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Metabolism in Diabetes Mellitus

BY

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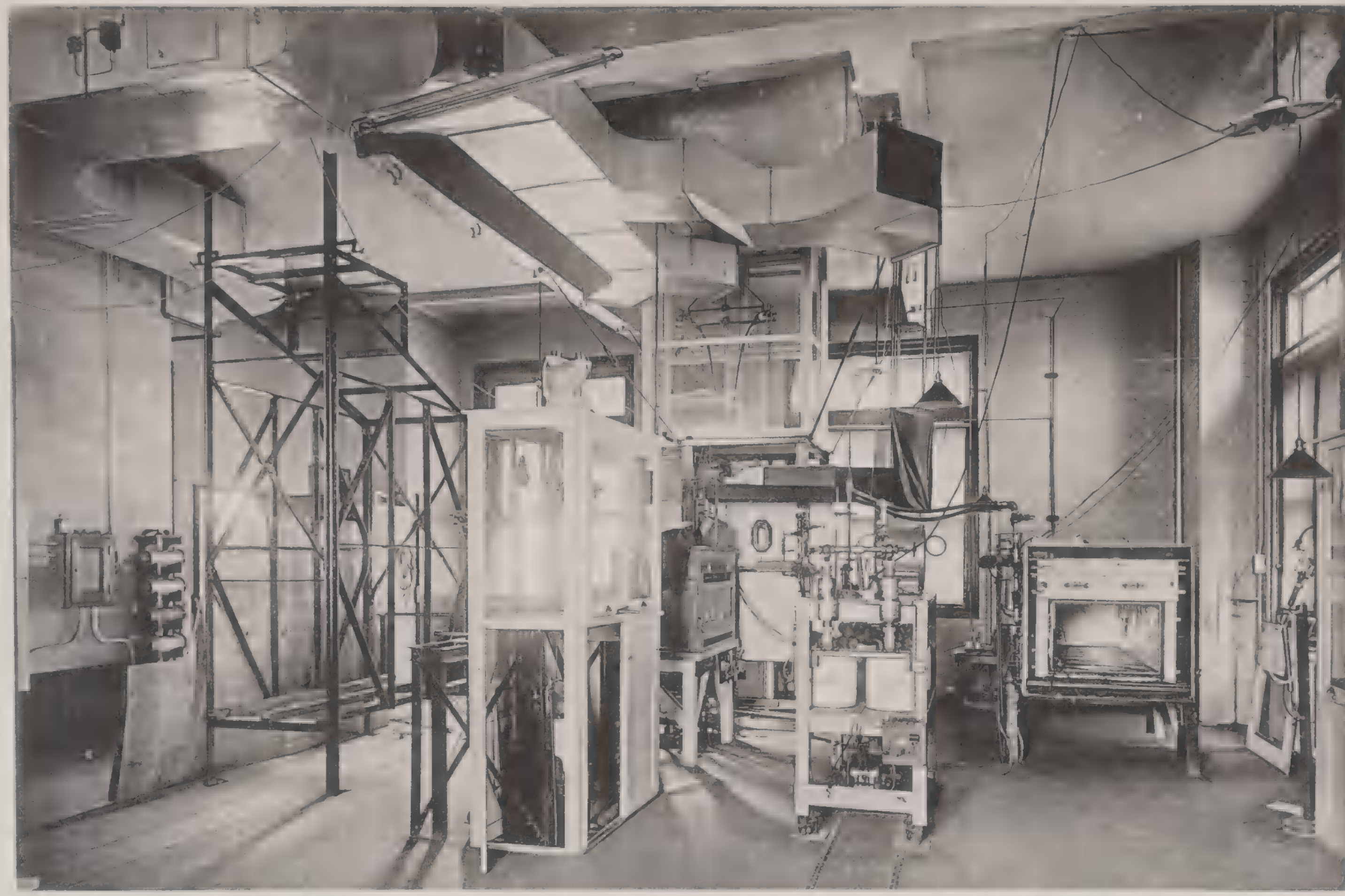

GENERAL VIEW OF THE RESPIRATION CALORIMETER LABORATORY.

In the center is the food aperture of the chair calorimeter and above is the galvanometer hood used in connection with the observer's table, at the left of the food aperture. To the right of this is the movable table with apparatus for maintaining the ventilation and for absorbing the water vapor and carbon dioxide from the air-current. At the right is the bed respiration calorimeter. In the center of the foreground is the balance for weighing apparatus upon the absorber table. At the left is the structural steel framework of the respiration calorimeter for various kinds of muscular work.

PREFACE.

In establishing the Nutrition Laboratory in Boston, the design was not only to continue the researches begun at Wesleyan University on the metabolism of normal individuals, but to still further extend these researches so as to include studies of pathological metabolism. The metabolism in diabetes mellitus was first selected for such investigation and the experiments here reported represent the progress thus far made in this study.

In collaboration with Dozent Dr. Falta of Vienna, we began experiments upon the metabolism of diabetes mellitus in October, 1908. The chief point of the investigations was to determine whether the metabolism of severe diabetics at rest was increased above the normal. The investigations thus performed in common are represented by experiments Nos. A 1 and A 2 and A 10 to A 13 with Case A, experiments Nos. E 1 to E 4 with Case E, and experiments Nos. F 1 and F 2 with Case F. Since it is difficult (by correspondence) to arrive at an understanding about details of explanation and description of the experiments, we all have agreed, in order not to delay still further the publication of the work, to publish separately the experiments which were jointly carried out. Dozent Falta, in the Zeitschrift für klinische Medizin, will shortly present and discuss in detail the experiments mentioned above. Obviously these experiments form but a relatively small proportion of the material we present in this report, and, as is to be expected, the larger amount of data has materially influenced our view-point. Consequently, in individual details, our opinions may differ, but upon the chief point, the increase in the metabolism at rest of severe diabetics,[1] we are agreed.

In the experimental part of this research and the computation and the preparation of the material for publication, we have enjoyed the active cooperation of a large number of associates. The experiments were for the most part under the direct supervision of Mr. T. M. Carpenter, of the Nutrition Laboratory staff. In this experimental work he was ably assisted by Messrs. L. E. Emmes and J. A. Riche. The determinations of ammonia and β-oxybutyric acid, and the determinations of the sugar by polarization were made either by Miss Elsie Newman in a private laboratory (E. P. J.) or by Dr. F. A. Stanwood in the Laboratory of Biological Chemistry of the Harvard Medical School. The total nitrogen deter-

[1] In a preliminary publication (not previously submitted to us) which Dozent Falta personally made at the Congress for Internal Medicine in Wiesbaden, 1909, by a misunderstanding upon his part, incorrect figures were used for the metabolism at rest of normal individuals. In the more extensive publication of Dozent Falta, correct figures will be given.

minations and the sugar by the Citron test were made by Miss Alice Johnson and Miss Hope Sherman in the Nutrition Laboratory.

The intelligent dietetic handling of the patients was secured through the active cooperation of Miss Zilla McLauchlin, of the New England Deaconess Hospital.

The histories and notes upon three of the patients before and after the period they were under our observation were most kindly put at our disposal by Dr. Harry W. Goodall, Dr. Theodore C. Janeway, and Dr. George Carroll Smith.

The report has received the helpful editorial criticism of Miss A. N. Darling, and the computations and tabulations have been for the most part under the direction of Mr. W. H. Leslie, who was assisted in this work by Messrs. H. L. Higgins and A. G. Emery and Miss F. E. Kallen, Miss P. H. Colbeth, and Miss K. E. Murphy.

To all of these co-workers in this investigation we wish to express our thanks and deepest appreciation of their sincere interest and untiring assistance.

NUTRITION LABORATORY, CARNEGIE INSTITUTION OF WASHINGTON,
Boston, Mass., April 15, 1910.

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1

PART I.

INTRODUCTION.

Perhaps no chronic disease makes such rapid inroads on health, strength, and weight as does diabetes. The large amounts of sugar in the urine, the polydipsia, polyphagia, and polyuria are observations so common in many cases that it is not at all surprising that the gross metabolism during diabetes should have been studied by many investigators.

EARLIER INVESTIGATIONS ON GROSS METABOLISM IN DIABETES.

In the earlier investigations on metabolism in diabetes, two types of apparatus have been employed, the respiration chamber and the mouth-breathing appliance. The conditions obtaining in studies with these two types of apparatus are quite different. In the respiration chamber the subject is sitting up or lying in bed under conditions of normal rest, although there is more or less muscular activity. With the mouth-breathing appliance, on the other hand, he is lying quietly under almost enforced muscular rest, with a minimum amount of exertion.

The conditions vary so widely, especially with regard to muscular activity, that it is usually not practicable to compare these two classes of experiments with any degree of satisfaction. It has been shown, however, in a large number of experiments at Wesleyan University, that the results obtained for the carbon-dioxide elimination and the oxygen consumption during the period when the subjects are in the respiration chamber and asleep may be compared with those obtained by the use of the special mouth-breathing appliances, particularly the Zuntz-Geppert apparatus.[1] In considering the results of the earlier studies made on the metabolism in diabetes, we will therefore first take up those experiments carried out by the chamber method, and while experiments with the Zuntz-Geppert apparatus were made as early as 1891, the discussion of the results thus obtained will be deferred until all researches with the chamber method are presented.

INVESTIGATIONS MADE BY THE RESPIRATION CHAMBER METHOD.

The large respiration chamber of Pettenkofer,[2] which was constructed in Munich in 1862, was the first apparatus of this type with which experiments on diabetes were made, and as used by Pettenkofer and Voit ordinarily gave remarkably satisfactory and accurate determinations for the carbon-dioxide excretion of man.

[1] Benedict and Carpenter, Carnegie Institution of Washington, Publication No. 126, pp. 166 and 182. See also Durig, Physiologische Ergebnisse der im Jahre 1906 Durchgeführten Monte Rosa-Expedition. Ueber den Erhaltungsumsatz. Besonders Abgedruckt aus dem LXXXVI. Bande der Denkschriften der Mathematisch-Naturwissenschaftlichen Klasse der Kaiserlichen Akademie der Wissenschaften. Wien, 1909.

[2] Pettenkofer, Ann. der Chem. u. Pharm., 1862, Supp. Bd. 2, pp. 1-52.

Certain fundamental errors entered into their determination of the water vaporized, and the determinations of the oxygen consumption of man were of necessity confined to those made by the indirect method, hence all the errors incidental to the determinations of the carbon-dioxide elimination, water vaporization, and changes in body-weight affected the results for the oxygen consumption. A critical examination of their data shows that while we can rely for the most part upon the determination of the carbon-dioxide elimination, little reliance can be placed on the determination of the water-vapor and practically none upon that for the oxygen consumption.

Until very recently the oxygen consumption of a subject experimented upon in the respiration chamber could only be determined indirectly, but the direct determination of this factor has also now been made possible. The method used for the indirect determination of the oxygen consumption may be expressed by the formula $a = b + c - d$, in which a is the amount of oxygen consumed out of the air, b the carbon dioxide produced, c the water vaporized, and d the loss in weight of the body expressed in grams. The determination of the oxygen consumption by this method, therefore, involves an extremely accurate knowledge of these factors. A recent article by one of us [1] has considered in great detail the difficulties incidental to a careful and accurate determination of the indirect method of determining the oxygen consumption, particularly in experiments on man. With experiments on small animals, Haldane [2] has developed this method to the highest degree of perfection so that it is possible to weigh not only the animal but also the total respiration chamber itself. With man, however, it is necessary to weigh the body of the man while inside the respiration chamber, and the hygroscopic nature of the bed and bedding, furniture, etc., necessitates an accurate record of the changes in weight of this material, also.

As a result of a large number of 24-hour experiments in the respiration apparatus at Wesleyan University, it was found that an accurate determination of the oxygen consumption by the indirect method was extremely difficult. The amount of furniture and hygroscopic material in the Wesleyan University chamber was very much less than that inside the chamber of Pettenkofer and Voit and provision was made, also, for weighing the subject, furniture, bedding, etc., in the chamber by means of scales outside. Even with these more modern appliances, however, it was found 40 years after the experiments of Pettenkofer and Voit that the indirect determination of the oxygen consumption still remained an extremely difficult task, and only by the expenditure of a large amount of time in the development of special technique and special appliances has it been possible to carry out with man a few experiments in which a comparison has been made of the direct and indirect methods for determining the oxygen consumption. Fortunately it has been possible to prove that under these extraordinary conditions as to technique and apparatus the indirect determination of the oxygen

[1] Benedict, Am. Journ. Physiol., 1910, **26**, p. 15

[2] Haldane, Journ. Physiol., 1892, **13**, p. 419.

consumption agrees with the direct determination, though experience with both methods has shown that only the direct determination is practicable in researches on the metabolism of man.

In 1867, Pettenkofer and Voit[1] made the first notable contribution to the study of total metabolism in diabetes, in which they gave the results of a series of experiments on a young man with severe diabetes. The subject was 21 years old and had formerly worked on a farm. Between August, 1865, and August, 1866, seven 24-hour experiments were made with him, in which the total intake and output were measured, and complete analyses made of the food, feces, urine, and respiratory products, including an indirect determination of the oxygen consumption. The experiments are not numbered in chronological order but the first experiment reported by them was the fasting experiment of February 1, 1866. In order to make the fast as little trying as possible for the subject, they administered 35.9 grams of meat extract with 22.3 grams of salt and 2590 grams of water. All the other experiments were made with diets varying in the amount of protein and in the total amount of food ingested. The results of the seven experiments are given in table 1.

TABLE 1.—*Measurements of metabolism in respiration experiments on a diabetic.*
[Pettenkofer and Voit.]

Experiment No. and date.	Body-weight.	Kind of experiment.	Carbon dioxide.	Water.	Oxygen.
	kilos.		*grams.*	*grams.*	*grams.*
I. Feb. 1, 1866....	54.5	Fasting	[1] 502	[1] 721	[1] 344
II. Aug. 7, 1865....	55.0	Heavy mixed diet.	795	759	792
IV. Dec. 27, 1865....	54.5	Average diet	621	764	680
VII. Jan. 9, 1866....	53.0	Protein-free diet ..	618	762	610
VIII. Jan. 19, 1866....	52.0	Protein-rich, carbohydrate-free.	629	658	613
X. Aug. 10, 1866....	52.0	Mixed diet	659	612	572
Day	52.0	......Do..........	359	278	246
Night	52.0	......Do..........	300	303	294
XI. Aug. 14, 1866....	51.0	......Do..........	660	649	578
Day	51.0	......Do..........	345	358	282
Night	51.0	......Do..........	315	291	296

[1] For the relation between the total amount per day and the calculated amount per hour and per minute and per kilogram, see table 168b, page 175.

An examination of these experiments shows that insufficient data are recorded with regard to the muscular activity of the subject inside the chamber. The young man was unquestionably in a weakened condition and did not move about to any great extent. Nevertheless, knowing, as we do to-day, that minor muscular movements play an important rôle in the metabolism and that a rest, even in bed, may not indicate a uniform muscular condition from day to day, certain differences in the experiments may easily be due to such minor muscular movements. Even in the two 24-hour experiments which were divided into day and night periods, we are not certain of the uniformity of the muscular activity during the

[1] Pettenkofer and Voit, Zeitschr. f. Biol., 1867, **3**, pp. 380–444.

night period when the subject was unquestionably in bed. He may or may not have been asleep, and if not asleep the muscular activity might have been considerable, although the uniformity of the carbon-dioxide excretion furnishes some evidence in support of the view that the muscular activity was the same in both periods.

An examination of the data regarding the oxygen consumption shows that, in the fasting experiment, Pettenkofer and Voit compute that the subject used only 344 grams of oxygen. Other values found for the successive experiments were 792, 680, 610, 613, 572, and 578 grams, respectively. Although these figures agree with reasonable regularity among themselves and are probably not very far from the correct values, nevertheless an examination of the figures given for the day and night periods in the last two experiments shows the difficulty of utilizing the indirect method for determining the oxygen consumption. Thus, in the experiment on August 10, 1866, it was computed that there were 246 grams of oxygen consumed in the day and 294 grams at night. In the experiment on the 14th of August of the same year, it was computed that there were 282 grams of oxygen consumed in the day and 296 grams at night. This greater absorption of oxygen in the night is contrary to all subsequent experience with respiration experiments.

While it is certain that the determinations of the carbon-dioxide elimination by means of their apparatus were liable to an error not greater than 3 per cent, there are large errors possible in the determination of the water vaporized, and this would consequently affect the indirect determination of the oxygen intake. This feature has been considered in a special discussion by Voit,[1] and consequently it is fair to consider that many of the deductions of these writers as a result of the apparent demonstration of the storage of oxygen during the night are based upon a false conception, and no reliance whatever should be placed upon the values found for oxygen consumption.

On the other hand, it is a most striking demonstration of the painstaking care and the ingenuity of the apparatus and methods devised by these pioneers, that the values for carbon-dioxide elimination show such striking uniformity and agree with practically all recent research. The well-known increase in metabolism as a result of the ingestion of food, particularly a diet rich in protein, is clearly shown in the results as presented by these writers.

Unfortunately, placing the greatest stress upon the determination of the oxygen consumption, these authors in the first presentation of this work, drew erroneous conclusions, which have subsequently been revised by Voit himself.[2] Unfortunately, also, in this treatise on physiology, Voit leaves some doubt since a number of conflicting statements with regard to the absorption of oxygen by these diabetics find a place in this discussion.

To interpret the metabolic transformation in experiments with diabetics, it is necessary to compare them with the results of experiments with normal individ-

[1] C. and E. Voit and J. Forster, Zeitschr. f. Biol., 1875, **11**, p. 126.
[2] Voit, Hermann's Handbuch der Physiologie, 1881, **6**, p. 228.

uals made under similar conditions. It is impossible to compare directly results obtained with one type of respiration apparatus under certain body conditions in respect to muscular activity, state of digestion, etc., with experiments made with another type of apparatus under entirely different physical conditions. For such comparison, Pettenkofer and Voit unfortunately selected experiments made by themselves a few years prior on a large, robust workingman, weighing some 70 to 80 kilograms. Without giving due consideration to the difference in body-size, the enormously decreased metabolism as shown by the diabetic subject led to erroneous assumptions and deductions on the part of these writers. Fortunately, these investigators previously made an experiment with a man of much weaker frame but with a body-weight of 53 kilograms, which was essentially that of the diabetic. This man, with an average diet, eliminated 695 grams of carbon dioxide, while on a similar diet the diabetic subject produced 621 grams. Computed on the basis of per kilogram of body-weight, we see that the diabetic eliminated 11.39 grams of carbon dioxide per kilogram and the normal man 13.11 grams in 24 hours.

The difficulties of comparing these experiments have already been pointed out and even if the comparisons were reliable on the basis of per kilogram of body-weight, we still have differences in minor and, indeed, major muscular activity. For example, it is unquestionably true that with the robust workingman, with whom the diabetic subject was compared, there was much more muscular activity inside of the chamber than with the emaciated, weak diabetic. Too little evidence is given by the writers regarding the muscular activity of the 53-kilogram man as compared with the diabetic. It is plain, therefore, that we must take these values of Pettenkofer and Voit with a certain degree of reserve. Nevertheless, when compared with normal individuals experimented on in the respiration chamber, the results are not abnormal and, indeed, we have every reason to believe that the deductions drawn by Pettenkofer and Voit to the effect that the diabetic required much less oxygen and gave off much less carbon dioxide than does a normal healthy individual, are not true. If the diabetic and normal subjects had had the same body-weight and approximately the same muscular activity, we believe that no material differences in the carbon-dioxide excretion would have been observed.

For more than 20 years following the Pettenkofer and Voit publication, no researches on the total gas exchange or energy transformation of diabetics were made, but in 1889, Livierato[1] published a series of experiments with diabetics in which a Pettenkofer respiration chamber was used. Great reluctance has been exhibited on the part of recent writers to accept any of the results reported by Livierato, and it is not at all surprising, since by the simple addition of small amounts of sodium bicarbonate or lactic acid to the diet, enormous increases in carbon-dioxide excretion per hour are reported by this writer—increases amounting to several hundred per cent. The rather meager statements of Livierato

[1] Livierato, Archiv f. Exp. Pathol. u. Pharm., 1888–89, **25**, p. 161.

would imply that the experiments were of but 1 hour's duration, and possibly less than an hour. No indication whatever is given of the degree of muscular activity of the subjects inside the chamber or of their body position, and it is doubtless true that in certain of the experiments, the very large variations in carbon-dioxide production can not possibly be ascribed to the small amounts of sodium bicarbonate or lactic acid given. Furthermore, that they can be logically ascribed to variations in muscular activity is highly improbable, and it would appear as if there were some gross error in the technique affecting these results.

Examining an earlier research [1] of Livierato, on the influence of certain antipyretics, we find a large number of experiments, each of 1 hour or less, in which the results indicate enormous differences in the carbon-dioxide excretion per kilogram of body-weight per hour. Nevertheless, in none of these experiments do we find the variations reported by Livierato in diabetes, and many of the experiments in this research gave values for the resting metabolism per kilogram of body-weight that are fully in accord with the data obtained in the best recent work. It is highly probable, therefore, that many of the results obtained by Livierato on diabetics are of sufficient accuracy to be considered as representing the actual conditions. It is likewise certain that a number of them must be discarded owing to gross errors in technique.

Livierato's first experiment on a diabetic was with a man 40 years of age, weighing 52 kilograms. With 11 liters of urine per day and nearly 700 grams of sugar, the carbon-dioxide production per hour was 20 grams. A second experiment followed a period of 6 or 7 days, during which the diet contained large quantities of meat and cheese. The body-weight was 50.5 kilograms, and with 4 liters of urine and 168 grams of sugar there was a carbon-dioxide production per hour of 20.6 grams. With but a slight change in the diet, a second series of experiments showed 29.9 grams of carbon dioxide per hour. Still another test with a preceding diet of 8 days containing 1800 grams of meat, 50 grams of cheese, and 2.5 liters of 20 per cent alcohol solution, and with a body-weight of 51.6 kilograms, the carbon-dioxide production per hour was 26.8 grams. By adding vegetables to this diet, he obtained 27.6 grams of carbon dioxide per hour, and with 8 grams of sodium bicarbonate and artificial Karlsbad water, he obtained 33.8 grams per hour. With a diet containing 500 grams of meat, eggs, vegetables, sodium bicarbonate, and Karlsbad water, the body-weight being 52.4 kilograms, he obtained 51 grams of carbon dioxide per hour. Adding to this diet 1 liter of milk and still continuing the sodium bicarbonate and Karlsbad water, the carbon dioxide became 33.5 grams with a body-weight of 53.1 kilograms. Substituting 3 grams of lactic acid for the sodium bicarbonate and the Karlsbad water in this diet, with a body-weight of 52.8 kilograms, the carbon-dioxide elimination increased to 48.8 grams.

When the milk was omitted from this diet, the carbon-dioxide elimination was 50.1 grams per hour, with a body-weight of 52.8 kilograms. With a body-

[1] Livierato, Modo di Comportari del ricambio materiale sotto l'Azione di diverse sostanze antipyretiche. Revista Clinica di Bologna, 1885, **5**, p. 748.

weight of 55.2 kilograms and a diet of meat, eggs, bread, vegetables, and 3 grams of lactic acid, he obtained an elimination of 36.8 grams of carbon dioxide per hour. With the same diet as above, but adding 8 grams of sodium bicarbonate, with a body-weight of 56.3 kilograms, 39 grams of carbon dioxide were eliminated per hour. It is highly probable that all values obtained above an elimination of 35 grams of carbon dioxide per hour with this subject at rest are due to errors in experimental technique, as it is hardly conceivable that there could be sufficient differences in muscular activity to account for the differences in the carbon-dioxide production.

In the second case with a 60-year old woman, Livierato obtained with a normal diet an elimination of 14 grams of carbon dioxide per hour. In other experiments, there was a production of 14.6 and 14.1 grams, respectively. By the addition of small amounts of sodium bicarbonate, he obtained an increase to 26.7 grams, and after the addition of 1 liter of milk to the diet, the enormous amount of 38.4 grams were eliminated. Lactic acid substituted for sodium bicarbonate resulted in a production of 26.9 grams of carbon dioxide, and with an ordinary diet containing 850 grams of meat, 150 grams of bread, 1.5 liters of wine, and 3 grams of lactic acid, the carbon-dioxide elimination was 28.3 grams. These experiments were discontinued as the patient developed pneumonia.

The third case was with a girl 19 years old who had had diabetes for 4 years. At the beginning of the experimenting the carbon-dioxide production was 16.7 grams and increased with alkali treatment to 32 grams in one experiment and to 33 grams in another. In still other experiments with the same girl, the alkali treatment seemed to produce similar enormous influences on the carbon-dioxide output.

An examination of the results obtained by Livierato without treatment of alkali or acid shows that the values are usually well within the limits of the carbon-dioxide production of diabetics. It is thus impossible to explain the variations in the carbon-dioxide production apparently resulting from the ingestion of relatively small amounts of sodium bicarbonate or lactic acid, and while the almost conclusive evidence of gross errors in the experimental technique tend to vitiate the values of the research as a whole, it is highly probable that in a number of the experiments values were obtained which were truly indicative of the metabolism under the experimental conditions.

Appreciating the significance of the determination of oxygen in experiments with diabetics, Weintraud, a former student of Naunyn, and Laves [1] in 1894 carried out a series of researches on diabetes in the Hoppe-Seyler respiration apparatus, then recently completed in the laboratory at Strasburg. The subject of these experiments was the one formerly used in a long series of digestion and dietetic experiments made by Weintraud, in which apparently enormous variations in the energy requirement, as measured by the food eaten and changes in body-weight, were noted at different periods.

[1] Weintraud and Laves, Zeitschr. f. physiol. Chem., 1894, **19**, p. 603.

The Hoppe-Seyler respiration apparatus marked a most important step in the determination of the physiological factors of metabolism. Unfortunately, in the original description of this apparatus[1] no particulars are given with regard to the control experiments, so we have no means of judging as to the accuracy of the apparatus.

The series of experiments by Weintraud and Laves with the diabetic gave a number of most interesting results. In all, five experiments are reported. In the first experiment, which lasted from $10^h\ 15^m$ a. m. to $7^h\ 56^m$ p. m., the carbon-dioxide production and oxygen consumption per kilogram of body-weight and per minute were 4.425 c. c. and 6.23 c. c., respectively. The respiratory quotient was 0.7. In the second experiment, which extended from $10^h\ 15^m$ a. m. to $7^h\ 52^m$ p. m., the amounts were 3.795 c. c. and 6.164 c. c., respectively. The respiratory quotient was 0.617. In the third experiment, the period was from $9^h\ 48^m$ p. m. until $7^h\ 13^m$ a. m., and the values were 3.65 c. c. and 5.744 c. c., respectively, with a respiratory quotient of 0.64. In the fourth experiment, which extended from $10^h\ 15^m$ p. m. until $7^h\ 15^m$ a. m., there were 3.901 c. c. of carbon dioxide and 5.593 c. c. of oxygen per kilogram per minute, and the respiratory quotient was 0.699. In the fifth experiment, from $9^h\ 35^m$ a. m. to $6^h\ 35^m$ p. m., the values were 4.109 c. c. and 5.53 c. c., respectively, with a respiratory quotient of 0.742.

In all of these experiments the subject remained sitting quietly in a chair inside of the respiration chamber. In the third and fourth experiments he undoubtedly slept most of the time. Food was taken during the progress of the first experiment, also shortly before the second experiment, and 5 hours before the third experiment. In the fourth experiment a part of the food was eaten before and a part during the experiment. The diet on this day included 200 grams of levulose, while in the three preceding experiments the diet was practically carbohydrate free. In the fifth experiment, the subject ate immediately before the experiment, and during the experiment considerable amounts of bread were taken which resulted in the ingestion of 314 grams of carbohydrate calculated as sugar. The values for the carbon-dioxide elimination found in these experiments are not unlike those that would be expected with normal individuals; on the contrary, the values for the oxygen consumption are abnormally high and have been subject to much criticism. The absence of control experiments makes criticism of the accuracy of the oxygen determinations very difficult.

In support of his theory that the excretion of sugar in diabetes is due in large part to the diminished carbon-dioxide output, Ebstein[2] made a series of experiments in a Pettenkofer respiration apparatus in connection with the Agricultural Experiment Station at Göttingen, with the cooperation of Franz Lehmann. The subject, who weighed, without clothing, 56.8 kilograms, had a mild form of diabetes, and the diet was not free from carbohydrate. From the 24th to the 25th of July and from the 26th to the 27th of the same month, the carbon-dioxide output

[1] Hoppe-Seyler, Zeitschr. f. physiol. Chem., 1894, **19**, p. 574.
[2] Ebstein, Deutsch. med. Wochenschrift, 1898, **24**, p. 101.

of this man was determined in two 24-hour experiments. In the first experiment, 705.3 grams, and in the second, 670.2 grams, of carbon dioxide were found. Ebstein concluded that these values agree perfectly with those found by Pettenkofer and Voit, and Weintraud and Laves, and substantiate his theory that the diminished carbon-dioxide elimination is an important factor in diabetes.

In an extensive investigation on the influence of the ingestion of carbohydrate on the carbon-dioxide excretion, Johansson,[1] using the Sondén-Tigerstedt respiration apparatus in Stockholm, made a series of experiments with 4 diabetics. The experiments were so arranged that the experimental periods were of 1 hour's duration, and the subjects were at complete muscular rest. At the beginning of the first hour, the subject took 48.5 grams of dextrose in 100 grams of water. For comparison, the carbon-dioxide production of these individuals was determined 12 hours after the last meal.

The first case, a man 52 years of age, with a body-weight of 61.8 kilograms, and height of 169.5 centimeters, was evidently a light one, and it frequently happened that the subject was sugar-free. Two experiments showed that he eliminated in 1 hour 18.9 and 19.3 grams, respectively, of carbon dioxide. After the ingestion of dextrose, the carbon-dioxide excretion increased to 22 or 23 grams, but rapidly diminished and at times was actually less than that found when no dextrose was given, particularly during the fourth or fifth hour. But a small proportion of the ingested dextrose was found in the urine.

The second case, a man, 65 years of age, with a body-weight of 85 kilograms, and 156.5 centimeters high, had had the disease since 1900. Two 2-hour experiments without food showed that this man excreted in the first hour 24 grams and in the second, 22.4 grams of carbon dioxide; in the second experiment he eliminated 24.9 grams in the first hour and 24.8 grams in the second. The ingestion of dextrose did not influence the carbon-dioxide elimination in any way, and but a small proportion of the dextrose ingested was subsequently discovered in the urine.

With the third case, a woman, 68 years of age, weighing 43.4 kilograms, and 152.7 centimeters high, the disease was first identified in 1900, and in 1904 she had an attack of diabetic coma. A 2-hour experiment without food showed that her carbon-dioxide production was 16.6 grams in the first hour and 15.6 grams in the second. After the ingestion of 50 grams of dextrose or levulose, there was no material increase in the carbon-dioxide production.

The fourth case was that of a woman, 71 years of age, weighing 54.4 kilograms, and 144.5 centimeters high. She had had diabetes for 10 years. One experiment of 2 hours without food showed an excretion of 18.4 grams of carbon dioxide in the first hour and 19 grams in the second hour. After the ingestion of 60 grams of dextrose or levulose, there was but little, if any, change in the carbon-dioxide production. It was impossible to recover all of the ingested sugar in the urine.

[1] Johansson, Skand. Archiv f. Physiol., 1908, 21, p. 1.

Recently Dubois and Veeder,[1] working under the direction of Dr. Brugsch, of the II Medical Clinic, Berlin, have reported a series of respiration experiments with diabetics in a Pettenkofer respiration chamber constructed after the plan of Rubner. Experiments were made with a normal individual and also with two cases of diabetes, one of which was a severe and the other a light case. The normal individual, 27 years of age, weighed 70.1 kilograms and excreted 783.8 grams of carbon dioxide in 24 hours, and the heat elimination was calculated to be 32.7 calories per kilogram of body-weight. With the diabetic, 23 years of age, and a weight of 70.4 kilograms, the total carbon-dioxide output per 24 hours was 748.8 grams. The heat elimination was calculated to be 34.3 calories. The third subject with light diabetes was 39 years of age and weighed 68 kilograms. The carbon-dioxide excretion was 778.4 grams in 24 hours and the heat elimination was calculated to be 31.7 calories per kilogram of body-weight. A summary of the three cases is given in table 2.

TABLE 2.—*Results of experiments on diabetics made by Dubois and Veeder.*

	Weight.	Total carbon dioxide.	Calories.	Calories per kilogram.	Carbon dioxide per kilogram per minute.
	kilos.	*grams.*			*c. c.*
Normal	70.1	783.8	2295	32.7	3.95
Severe diabetes	70.4	748.8	2453	34.3	3.75
Mild diabetes	68.0	778.4	2258	31.7	4.04

The authors took the precaution to test the accuracy of the apparatus by making a number of experiments in which different weights of candles were burned, and the results were very satisfactory. The apparatus and method have been described by Steyrer.[2]

INVESTIGATIONS MADE WITH MOUTH-BREATHING APPLIANCES.

Practically all of the work on diabetes involving the use of a mouth-breathing appliance has been carried out with the Zuntz-Geppert apparatus. The first research of any importance was that of Leo[3] who experimented with five different diabetics and made a number of experiments with each individual 12 hours after the last meal had been taken. The author had been trained in the Zuntz laboratory and consequently his experiments were carried out with the greatest exactness and care. A summary of the results expressed as cubic centimeters per kilogram and per minute, are given in table 3.

The author concludes that diabetes can not influence in any material way the total metabolism so far as the total energy transformation for the day is concerned. Experiments on the ingestion of carbohydrates showed that even in the

[1] Dubois and Veeder, Archives of Internal Medicine, **5**, 1910, p. 37.
[2] Steyrer, Ueber den Stoff- und Energieumsatz bei Fieber, u. s. w. Ztschr. f. exp. Path. u. Therap., 1907, **4**, p. 720.
[3] Leo. Zeitschr. f. klin. Med., 1891, **19**, p. 101.

most severe form of diabetes, a not inconsiderable quantity of sugar ingested in the food was actually burned. For all five patients, there was an increase in the gas exchange after taking food.

TABLE 3.—*Results of experiments on diabetics made by Leo.*

Subject.	Carbon dioxide.	Oxygen.
	c. c.	c. c.
Kr.	3.21	4.01
Kord.	2.88	3.87
Feib.	2.31	2.84
Fink.	2.80	3.48
Drag.	2.84	4.77

In 1894, Stüve,[1] also a pupil of Zuntz, reported two cases of diabetes in which he had determined the gas exchange by the Zuntz method. The oxygen consumption with one patient was 4.02 c. c. per kilogram of body-weight and per minute. With the second, at the time when the urine was free from sugar, the oxygen consumption was 3.96 c. c., and at the time when the sugar was excreted it was 4.13 c. c. The respiratory quotients for the two subjects were 0.73 and 0.74, respectively.

Since many of the previous experiments on diabetics had apparently indicated that the ingestion of carbohydrate usually produced some increase in the metabolism, Nehring and Schmoll[2] made a special study on the influence of carbohydrate on the gas exchange of two diabetics. Having studied in Zuntz's laboratory, they were thoroughly familiar with his technique. The first patient was especially well fitted for such experimentation as he had a very quiet respiration. He was 17 years old and was sugar-free at the time of the experiments. The body-weight, although not given by the authors, has been computed by Magnus-Levy to be 35 kilograms. An average of six observations with this subject showed the carbon-dioxide production per minute and per kilogram to be 3.3 c. c. and the oxygen consumption 4.48 c. c., with an average respiratory quotient of 0.744. The second patient was a woman, whose age was not given, and with a body-weight as calculated by Magnus-Levy of 74.2 kilograms. Two experiments with this patient showed an oxygen consumption per kilogram of body-weight of 3.70 c. c. and a carbon-dioxide production of 2.57 c. c., with an average respiratory quotient of 0.693. As the result of the ingestion of carbohydrate, the investigators found almost invariably a lowering of the respiratory quotient below the "nüchtern" value, the quotient returning to the normal "nüchtern" value only after some hours. The assumption is that there must have been a retention of carbohydrate in the body. The investigators conclude that the ingestion of carbohydrate has no influence on the digestive processes, and point out that while there are evidences that carbohydrates were not burned, at least during the first

[1] Stüve, Arbeiten aus d. städt. Krankenhause zu Frankfurt a. M., 1896.
[2] Nehring and Schmoll, Zeitschr. f. klin. Med., 1897, **31**, p. 59.

2 hours of the experiments, the increase in the metabolism can only be considered as a result of muscular work or of the work of digestion.

The observations of Robin and Binet[1] and those of Hanriot[2] are not accorded much value by writers, principally as a result of the technique. Their experiments, for example, indicate an enormous oxygen consumption under a condition designated by them as fasting and quiet, which of itself would be evidence of considerable muscular activity. These criticisms have been raised in extenso by Magnus-Levy.[3]

The experiments reported by Magnus-Levy,[4] one of the foremost technicians of the Zuntz school and a prolific writer on metabolism, have a peculiar interest and value. The experiments were all made under "nüchtern" conditions, *i. e.*, 12 hours after the last meal. Seven different subjects were used, on which, however, but four series were carried out with an accuracy satisfactory to the author himself. The first case, a man 43 years of age, weighing 62.2 kilograms, and 170 centimeters in height, showed an average carbon-dioxide production per minute and per kilogram of 3.24 c. c. and an oxygen consumption of 4.67 c. c. The respiratory quotient was 0.697. With a woman 35 years of age, weighing 33.8 kilograms and 145 centimeters high, the average of four experiments showed 3.72 c. c. for carbon-dioxide elimination and 5.17 c. c. for oxygen consumption, the respiratory quotient being 0.719. Both of these subjects had severe diabetes. The average of two experiments on a man with light diabetes, 71 years of age, weighing 91.5 kilograms, and 169 centimeters high, showed 2.04 c. c. for carbon-dioxide elimination and 2.82 c. c. for oxygen consumption. The respiratory quotient was 0.721. Three experiments on a woman with light diabetes, 69 years of age, 58.6 kilograms in weight and 154 centimeters in height, showed a carbon-dioxide elimination of 2.71 c. c. and an oxygen consumption of 3.88 c. c. The respiratory quotient was 0.698. With three other cases, Magnus-Levy obtained only one observation on each. One of these, a man 40 years of age and weighing 44 kilograms, showed a carbon-dioxide elimination of 3.74 c. c., an oxygen absorption of 5.88 c. c., and a respiratory quotient of 0.637. A woman with light diabetes, 56 years old and weighing 54.5 kilograms, showed 3.03 c. c. for the carbon-dioxide elimination, 4.73 c. c. for oxygen consumption and 0.640 as the respiratory quotient. In comparing his results with those of other writers and with those with normal persons, Magnus-Levy concludes that in all the experiments in which the subjects had severe diabetes there is a larger oxygen consumption per kilogram of body-weight.[5]

The most recent contribution to the study of the gas exchange of diabetics by means of the Zuntz-Geppert apparatus is that of Mohr.[6] The first patient was a woman 52 years of age, weighing 84.5 kilograms and 158 centimeters high. The

[1] Robin and Binet, Archive géner de medicin, 1898, **10**, p. 283.
[2] Hanriot, Comptes rendus, **114**, pp. 371 and 432.
[3] Magnus-Levy, Zeitschr. f. klin. Med., 1905, **56**, p. 86.
[4] Magnus-Levy, *ibid.*
[5] For Magnus-Levy's ingenious explanation of this point, see p. 163 beyond.
[6] Mohr, Zeitschr. f. exp. Pathol. u. Ther., 1907, **4**, p. 910.

average of the three experiments with this subject showed 2.29 c. c. of carbon dioxide eliminated per minute and per kilogram, and 3.16 c. c. of oxygen consumed with a respiratory quotient of 0.711. The second subject, with very severe diabetes, 11 years old and weighing 35 kilograms, without food, eliminated 4.68 c. c. of carbon dioxide and consumed 6.48 c. c. of oxygen, with a respiratory quotient of 0.723. These patients were also fed from 150 to 200 grams of meat and the gaseous exchange studied for periods following this of 3, 4, and 8 hours. In practically all of the experiments, there was a very great increase in the oxygen consumption, unaccompanied by an increase in the carbon-dioxide production 2 or 3 hours after taking the meat, resulting in an abnormally low respiratory quotient. Subsequently, the respiratory quotient increased to the former fasting value and, indeed, exceeded it in all cases in the seventh to eighth hour. The author concludes that although sugar or protein is still oxidized in the most severe forms of diabetes, the oxidation takes place much later and, in general, much slower than in a healthy man.

APPARATUS AND METHODS USED IN THE INVESTIGATIONS HERE REPORTED.

The apparatus used in connection with the experiments here reported was distinctly of special construction, and we believe that the methods have been so carefully controlled by check-tests as to insure the highest degree of accuracy for the apparatus employed. This bears particularly upon the method for determining the total carbon-dioxide output, oxygen intake, and heat elimination. Inasmuch as many of the methods employed in this investigation are of recent development, it is deemed advisable to give a brief description of them here.

DETERMINATION OF THE GASEOUS EXCHANGE WITH THE RESPIRATION CALORIMETER.

By far the larger number of experiments were made inside of a respiration chamber, which was designed to permit the determination of not only the carbon dioxide excreted but of the water vaporized, and more particularly of the oxygen consumed. The apparatus is constructed on the plan of the respiration calorimeter described by Atwater and Benedict,[1] but has been considerably modified and is described in its newer form in a more recent publication by Benedict and Carpenter.[2]

In this apparatus the subject sits or lies inside of a respiration chamber containing from 700 to 1400 liters of air, which is kept at a constant temperature of 19° to 20° C. By means of a rotary blower, the air is continually withdrawn from the chamber, passed through weighed vessels containing sulphuric acid to absorb the water-vapor, then through weighed vessels containing soda or potash

[1] Atwater and Benedict, Publication No. 42, Carnegie Institution of Washington, 1905.

[2] Benedict and Carpenter, Publication No. 123, Carnegie Institution of Washington, 1910.

lime to absorb the carbon dioxide, and finally through weighed vessels containing sulphuric acid to absorb the moisture yielded to the dry air by the soda-lime. The air, thus freed from water-vapor and carbon dioxide, is returned to the chamber to be breathed by the subject. The oxygen abstracted from the air by the process of metabolism is replenished by admitting pure oxygen from a previously weighed cylinder of the highly compressed gas. The increase in weight of the first water-absorber gives the approximate weight of the water vaporized during the experimental period, this period being usually 1 hour in length. The increase in weight of the soda or potash lime container, with its attendant water-absorber, gives the weight of the carbon dioxide exhaled, and the loss in weight of the oxygen cylinder shows the amount of oxygen absorbed by the subject.

Approximate values for the carbon-dioxide production, water vaporization, and oxygen absorption during the experimental period are thus obtained, but to be exact, fluctuations in the composition of the air inside of the chamber should be taken into consideration, and hence at the end of each experimental period an analysis of the air is made. For this analysis, a portion of the air-current, amounting to 10 or 20 liters, is deflected through three previously weighed U-tubes, the first containing sulphuric acid, the second, soda lime, and the third, sulphuric acid. From the increase in weight of the U-tubes and the relation of the volume of the sample to the total volume of residual air, the residual amounts of carbon dioxide and water can be determined. Since the residual air contains only nitrogen, oxygen, carbon dioxide, and water, the determinations of the carbon dioxide and water permit the computation of the combined volumes of nitrogen and oxygen with great exactness. Since the nitrogen is an unchangeable amount and none can enter or leave the chamber, obviously the amount of oxygen can be computed by deducting the volume of nitrogen in the chamber at the beginning of the experiment. By making these computations, it is easy to determine at the end of each experimental period the amount of carbon dioxide, water-vapor, and oxygen present in the air, and making due allowance for any variations in these amounts, the amount of water-vapor and carbon dioxide absorbed by the purifying vessels and the oxygen lost from the cylinder can be corrected for these fluctuations and thus a true measure obtained of the amount of carbon dioxide produced, water vaporized, and oxygen absorbed during the experimental period.

The apparatus has been subjected to the most rigid control tests and it has been frequently demonstrated that in experimental periods as short as 1 hour, it is possible to determine all three factors, carbon-dioxide production, oxygen absorption, and water vaporization to within an error of ± 1 to 2 per cent.[1] Usually the values found in the control tests are inside of this limit of error. Almost invariably in experiments of 3 to 5 hours' duration, the total sum of carbon dioxide produced and oxygen absorbed will be very close to theory.

In practically all of the experiments with diabetics it was possible to secure ex-

[1] Benedict, Riche and Emmes, Am. Journ. Physiol., 1910, **26**, p. 1.

periments of 2 or 3 hours or more in length. In nearly all cases it was also possible by means of the gas analysis apparatus, to divide the measurements into 1-hour periods, and hence the values are given in hourly periods as a general rule. The carbon-dioxide determination for such periods has been proved repeatedly to be extremely exact. On the other hand, the determination of the oxygen consumption and the apportionment of the oxygen for the different hours of an experiment continuing 2 or 3 hours may be somewhat at fault and occasionally abnormally high respiratory quotients have been obtained in one period and abnormally low quotients in the other, which would indicate a discrepancy in the oxygen measurement. *While as a rule, therefore, the oxygen determination for the whole experiment may be looked upon as exceedingly accurate, in many instances the values for the oxygen consumption in 1-hour periods may be at fault.* In general, however, we believe that the oxygen measurements as here reported in periods of 1 hour are well within the limit of error in physiological experimentation.

DETERMINATION OF THE GASEOUS EXCHANGE WITH THE RESPIRATION APPARATUS, USING NOSEPIECES.

The respiratory exchange can not be satisfactorily determined in extremely short periods by means of the large apparatus and certain problems can be better solved by having a more or less continuous study of the respiratory exchange over periods as short as 10 or 15 minutes. This has usually been accomplished in pathological cases by means of the Zuntz respiration apparatus, which has given such admirable results in the experiments of Magnus-Levy and others of the Zuntz school.

In connection with the development of the respiration chamber just described, it was found possible to adapt the same general principle for the determination of the respiratory gases to an apparatus which will not necessitate placing the subject inside of a respiration chamber. By means of a special form of nosepiece which will permit the collection of the expired air, the subject can lie comfortably on a couch in the laboratory, insert the nosepieces, and breathe without discomfort into the respiration apparatus, and by this method the total amount of carbon dioxide produced and oxygen absorbed during a period as short as 15 minutes may be accurately determined. The temperature of the room air in these experiments varies more or less, but it is usually between 15° and 25° C.

This apparatus, which has been described in detail elsewhere,[1] has likewise been subjected to most rigid tests by developing inside of a small supplementary chamber a known amount of carbon dioxide and absorbing a known amount of oxygen, and the results were most satisfactory. Further controls have been obtained in that subjects have first been tested upon the respiration apparatus, breathing through the nosepieces, and then immediately placed inside of a respiration chamber, where the respiration was perfectly normal, *i. e.*, without nose-

[1] Benedict, Am. Journ. Physiol., 1909, 24, pp. 345–374.

pieces. The respiratory quotients determined under those conditions were compared and the results have likewise been most satisfactory. A detailed account of these tests is given in the description of the respiration apparatus previously referred to. The practicability of the apparatus for experiments on pathological subjects has frequently been tested with both men and women, and so far as appears at present the apparatus is admirably fitted for this purpose.

METHOD OF DETERMINING THE TRANSFORMATIONS OF ENERGY.

For lack of sufficiently accurate calorimeters for use with man, no studies have previously been made in which the energy transformations of diabetics have been measured directly. The energy transformations have been computed in other experiments by means of the gaseous exchange and we believe that the experiments here reported are the first in which the calorimetry of a diabetic man has been studied by the direct method. The calorimetric features of this apparatus have been described in great detail in previous publications.[1] The respiration chamber is surrounded with a number of insulating walls which prevent the loss of heat by radiation, and different sections of the outer wall are arbitrarily heated or cooled so as to prevent any conduction of heat. To make the calorimeter adiabatic by this method, we resort to the principle of Rosa,[2] who employed a series of thermal junctions to indicate the temperature differences between the inner copper wall and the outer zinc wall. By connecting these thermal junctions with a delicate galvanometer, it is easy to determine whether the zinc wall should be heated or cooled in order to prevent conduction of heat into or out of the chamber. The heating of the zinc wall is accomplished by passing a current of electricity through resistance wires suspended in the air confined between the zinc wall and an insulating layer of hair felt. If, on the other hand, the zinc wall must be cooled, this is accomplished by passing a current of cold water through small brass pipes which are suspended parallel to the heating wires in the air space.

The larger portion of the heat given off by the subject is brought away from this perfectly insulated chamber by a current of cold water carried through a heat-absorbing system inside the chamber, consisting of a brass or copper pipe to which a large number of copper discs have been soldered to increase the area for the absorption of heat. Records are made of the temperature of the water as it enters and leaves the chamber, and the total mass of water passing through the chamber in the experimental period is measured by weighing the water on a platform scale. The average temperature rise, multiplied by the total quantity of water passing through the chamber, gives the amount of heat absorbed. By regulating the flow and temperature of the water entering the chamber, it is possible to bring away the heat as rapidly as it is liberated by the subject, and consequently the temperature of the calorimeter as a whole is held at a constant

[1] Atwater and Benedict, *loc. cit.* Benedict and Carpenter, *loc. cit.*
[2] Atwater and Rosa, Physical Review, 1899, **9**, pp. 129-163, and 214-251.

point. A certain portion of the heat, however, is used to vaporize the water from the lungs or skin of the subject, and hence it is necessary to know accurately the amount of water thus leaving the chamber in the form of water-vapor. This is accomplished by passing the total air-current, as previously stated, through a vessel containing strong sulphuric acid, and weighing the vessel at the beginning and end of the period. As each gram of water vaporized in the chamber requires for its vaporization 0.586 calories, it can easily be seen that the 25 to 30 grams of water ordinarily vaporized per hour results in an absorption of 13 to 16 calories, or from 20 to 30 per cent of the total heat elimination during an hour. By maintaining the calorimeter in an adiabatic condition and thus preventing the passage of heat into or out of the chamber through the wall, the total heat eliminated by man can easily be determined by adding the amount of heat required to vaporize the water leaving the chamber in the air-current to the amount of heat brought away by the water-current.

HEAT PRODUCTION AS COMPARED WITH HEAT ELIMINATION.

The large reservoir in the body for the storage or loss of heat makes it extremely difficult to differentiate between the heat production and the heat elimination of the body of a man during a given period, particularly during short periods. In the course of 24 hours the fluctuations in body-temperature are usually so regular that at any given time, especially during the sleeping period, the body-temperature is relatively constant, and an experiment beginning at 7 a. m. and ending at 7 a. m. the following day, before the subject has arisen from bed, gives us probably a very accurate measurement of the heat-production without recourse to a special measurement of body-temperature.

When the heat-production is computed in shorter periods, however, it is necessary to take into consideration the loss of material from the body, the changes in body-weight and in body-temperature. If the body has gained in weight 100 grams as the result of drinking a large amount of water, obviously the water has been warmed from the temperature at which it was consumed to body-temperature, and therefore heat has been absorbed. Conversely, if a large amount of urine has been passed, heat has been lost from the body in this way, and radiated and measured as heat eliminated, although not necessarily actually produced at the time. In certain experiments on healthy subjects it was possible to make the weighings quite frequently, but with diabetic patients this was not found feasible. From the exact measurement of the water vaporized, the carbon dioxide produced, and the oxygen consumed, as well as the true measurement of the urine voided, it is possible, however, to compute with great accuracy the actual losses in weight of the subject. These are taken into consideration in computing the heat production as compared with the heat elimination.

If a body weighing 70 kilograms loses 0.1° in temperature, it can be seen that if we assume the specific heat of the body to be 0.83, the heat lost from the body by cooling amounts to $70 \times 0.83 \times 0.1$, which equals 5.8 calories. This may

be from 5 to 8 per cent of the total heat-production during an hour. It is thus of the utmost importance to note the changes in body-temperature.

The measurements of the body-temperature have been made by two methods, sublingually or in the axilla with a clinical thermometer, and deep in the rectum by means of a specially devised electrical resistance thermometer. We have long since found that the ordinary clinical measurements as taken under the tongue are as a rule inadequate for our purpose. With the resistance thermometer, on the other hand, the body-temperature measurements can be made to 0.02° C. as frequently as desired by measuring the variations in resistance of the thermometer on a delicate Wheatstone bridge. The thermometer is of a pliable nature, and when inserted deep in the rectum its presence is not usually noticeable after a few moments. With this thermometer, therefore, it is possible to get most exact body-temperatures. With normal subjects undergoing long experiments, comparisons of heat-production and heat-elimination by means of these measurements are possible. With diabetics, especially when the patients are unfamiliar with the apparatus, it is often impracticable to use the rectal thermometer and sublingual measurements of body-temperature are then made with a clinical thermometer. In the respiration chamber, the air is kept at a constant temperature and approximates the ordinary air of a living room, so there is no tendency to cool the mouth and thus lower the sublingual temperature by rapid breathing due to excess cold or to physical exertion. The conditions depending upon the temperature of the air appear, therefore, to be favorable to an accurate measurement of body-temperature, even with a clinical thermometer; nevertheless, we recognize that the conditions are not ideal and we are not always certain of the accuracy of the measurements.

In previous publications, the term heat eliminated has been applied to the heat given off by the subject and measured by the apparatus, and this heat-elimination, when corrected for the changes in body-weight and body-temperature, and for the loss of heat in excreta, was designated as heat-production. In this report, however, it will be noticed that the heat actually recorded by the calorimeter, corrected for the known and readily measured factors, *i. e.,* the changes in body-weight, and the loss of heat in the urine excreted, is recorded as heat-elimination, while the term heat-production is applied only to this heat-elimination corrected for changes in body-temperature. By assuming accurate measurements of body-temperature, the heat-production can, therefore, be easily determined. Until more accurate observations of body-temperature, and particularly fluctuations in body-temperature, have been recorded, however, we can not use the heat-production as thus computed with the degree of assurance that we would wish. Consequently, in the tables and in all subsequent discussion we will make use of the values recorded as heat eliminated, giving in a footnote to each table the change in body-temperature during the experiment, and the heat-production for the total experiment as computed on this basis. The experiments here reported were rest experiments with the body activity at a minimum, and usually no food was taken,

so that the naturally occurring body-temperature fluctuations could not be so great as to seriously change the values for heat-elimination, particularly when computed on the basis of 6 hours or on the basis of per kilogram of body-weight per hour.

The normal fluctuations in body-temperature, as measured in the rectum by an electrical-resistance thermometer, have received a great deal of investigation in this laboratory and previously in the chemical laboratory of Wesleyan University.[1] Believing that a more accurate knowledge of topographical changes in the body is necessary, an extensive study of such changes of temperature has been begun in the Nutrition Laboratory. In this investigation an attempt will be made to compare the simultaneous fluctuations in temperature curves in different portions of the body and thus see if a 0.1° fall in temperature in the rectum, for example, corresponds to a 0.1° fall in temperature in the axilla or of the surface temperature. Until this investigation is completed and published, we must use the terms heat-elimination and heat-production with a certain reserve, for heat-production as here calculated is based upon the assumption that the changes in rectal temperature occurring in the course of 1 hour represent the changes in average temperature of the whole body.

ACETONE IN THE BREATH.

The general impression that large quantities of acetone are excreted in the breath of diabetics made it a matter of considerable moment as to the quantities that would be excreted while the subject was inside the respiration chamber. With the closed circuit of air in this chamber, there might be a tendency for the acetone to accumulate during the course of an experiment. On the other hand, all the air removed from the chamber by the ventilating air system passes through sulphuric acid twice and probably acetone would there be retained. At the end of each experiment, therefore, it was the rule, especially at the beginning of the investigation, to have the air inside the calorimeter chamber observed by a number of individuals. In no instance could any appreciable acetone odor be found and we have no reason to believe that acetone excreted in the breath played any important rôle in these experiments so far as the total metabolism or discomfort in the normal respiration of these patients were concerned. That there was acetone excreted in the breath may or may not be true, but certainly not enough was excreted to accumulate in the chamber and make it uncomfortable for the patient. Most of the experiments were performed with the subject fasting, and at such a time Folin has indicated that the so-called acetone odor is not apt to be present. Case I did not undergo an experiment at the time that the odor of acetone about him was so marked.[2] Similarly Grafe[3] was unable to detect a distinct acetone odor in the case of his fasting patient, although marked acidosis was present. His patient was not a diabetic, but the similarity between the acidosis of starvation and diabetes is universally acknowledged.

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[1] Benedict and Snell, Archiv f. d. ges. Physiol., 1901, **88**, pp. 492–500; *ibid.*, 1902, **90**, pp. 33–72. Benedict, Am. Journ. Physiol., 1904, **11**, pp. 145–169.

[2] See p. 126.

[3] Zeit. f. physiol. Chem., 1910, **65**, p. 21.

SUPPLEMENTARY APPARATUS.

STETHOSCOPE.

As an index of the total katabolism the pulse-rate, when properly taken, plays a rather important and suggestive rôle. The pulse-rate, as ordinarily obtained in a physician's office, or indeed, at the laboratory, may be subject to considerable fluctuations due to the psychical influence on the subject himself, but by attaching a Bowles stethoscope to the chest wall and listening to the heart beat through a long air-transmission tube passing through the metal walls of the chamber, it is possible to count the pulse-rate with a fair degree of regularity and entirely unknown to the subject. Under these conditions, a relatively accurate record of the pulse-rate during the experimental period can be obtained. The pulse is usually counted every 5 to 10 minutes by an observer outside the chamber and recorded in a book as the experiment progresses.

PNEUMOGRAPH.

The respiration-rate and the minor muscular movements were determined in these investigations by means of a pneumograph which was attached about the chest lightly and connected with a tambour and registering apparatus on the outside. The rise and fall of the tambour and the pointer gave the regular respiration-rate of the subject. Superimposed upon this movement of the tambour were major movements due to minor muscular movements other than the rise and fall of the chest. A curve or tracing was made on a smoked drum by the movement of the pointer, and from these pictures or curves can be obtained a fairly accurate idea of the relative muscular activity of the subject inside the chamber. Although the subjects were all supposed to be sitting quietly at rest, reading, nevertheless they differed noticeably at times in the amount of minor muscular activity indulged in.

SIGNIFICANCE OF PNEUMOGRAPH CURVES.

A specimen of a curve obtained by the pneumograph is given herewith (fig. 1). The smaller vibrations are those due to the ordinary rise and fall of the chest, while the larger vibrations are incidental to movements of the body, such as telephoning, collecting the urine, reaching to the floor for a book, turning the pages of a newspaper, or some similar minor movement. At no time did the subject leave the chair. As an aid to interpreting the significance of these movements, a second curve is reproduced (fig. 2), showing certain definite actions performed by one of the laboratory assistants, and giving a graphic representation of the influence of minor muscular activity.

The first curve given is the one obtained in experiment A 7, March 26, 1909, in which there were four 1-hour periods. The records for these periods have been placed in series and read from the top downward. As may be seen by the curve, during the first half of the initial period the subject was very quiet, but during the next 15 minutes, he was restless, and then quieted down for the re-

mainder of the period. Shortly after the beginning of the second period, the subject passed urine and the irregularity of the curve recorded by the tambour is very well seen in the portion for the first quarter of the second hour. During the rest of the hour, the subject was comparatively quiet with a few exceptions. At the beginning of the third hour he drank a cup of coffee, and this necessitated on his part a number of movements in order to get the bottle containing it. During the rest of the hour, as can be seen, the subject was very quiet. Throughout the fourth hour he was also very quiet, with the exception of about 10 or 15 minutes at the beginning of the period.

The second curve given was prepared especially as an aid in interpreting the records taken during the experiments. An assistant sat inside of the chair calorimeter with the pneumograph placed around his chest in the usual position and made the following movements at the direction of an assistant outside of the calorimeter:

(1) Sat perfectly still, reading; (2) crossed legs; (3) put leg back into normal position on the floor; (4) turned over a page in the book he was reading; (5) closed the book and dropped it to the floor; (6) took telephone and held it in position to talk; (7) returned the telephone to the hook; (8) took a urine jar from the floor and held it in his lap; (9) prepared to urinate; (10) urinated; (11) finished urinating and held the jar in his lap; (12) talked; (13) returned the jar to the floor; (14) took a bottle of water from the floor and drank from it; (15) returned the bottle to the floor; (16) yawned considerably; (17) leaned over the left arm of the chair and rested his head upon his left hand. The subject remained in this latter position until he left the calorimeter chamber.

In the intervals between the movements the subject sat perfectly quiet so that the records on the tambour for these intervals were due only to the normal respiration. As can be seen, the variations in the curve due to leaning over, reaching to the floor, and taking up the various articles are those which are more pronounced and more apparent. This coincides with the observations made in the experiments, as whenever the subject was requested to urinate or to drink from a bottle, there was usually a greater amplitude to the excursions of the pointer on the tambour.

A careful examination of all the curves obtained in these experiments shows three things: First, that with the same subject there is a remarkable uniformity in the hourly record of minor muscular movements other than respiration movements during the different experiments, indicating that the subjects in each experiment had practically the same degree of muscular activity. Second, noticeable variations in muscular activity are observed among the different subjects, some being considerably more restless than others. Finally, the normal individual, almost without exception, showed much greater muscular activity than did the diabetics. This last observation may have been due to the generally weakened condition of the diabetics and their indisposition to move about to any extent. It is not considered advisable to devote the time or to incur the expense

incidental to reproducing all of the curves secured in these experiments, but the conclusions given represent deductions drawn from a careful inspection of all the tracings.

URINE ANALYSIS.

The enormous amount of research on the analysis of urine, and particularly in regard to the analysis of diabetic urine, leaves very little to be contributed in an investigation of this nature. Since many of the researches on diabetics, however, have been carried out with urinary analytical methods that are distinctly clinical in nature, and hence of only approximate accuracy, we consider it of importance here to state exactly how these determinations were made and to point out some of the advantages in the methods employed.

DETERMINATION OF TOTAL NITROGEN.

The total nitrogen was determined by the method of Kjeldahl. By this method 5 c. c. of urine are digested with 20 c. c. of sulphuric acid and a small piece of copper wire weighing 0.10 gram. After heating slowly over the free flame to avoid frothing, the liquid is finally brought to a boil and the urine digested until colorless. The acid is then diluted with water, made strongly alkaline with caustic soda, and the liquid distilled in a still of special construction.[1] The ammonia is collected in standard hydrochloric acid and titrated with standard ammonia, using alizarine as an indicator. Frequent tests of the accuracy of the method as a whole were made by determining the nitrogen in chemically pure uric acid. The results show that the error in the nitrogen determinations is considerably inside of 1 per cent of the total nitrogen.

AMMONIA DETERMINATION.

The ammonia was determined by Folin's[2] method and was carried out practically as follows: Enough water was placed in the bottles used to receive the ammonia to cover the bulb; to this were added 6 drops of alizarine solution and then 20 c. c. of deci-normal sulphuric acid added. The bottles were then corked. Into each cylinder used, 10 c. c. of urine was pipetted and approximately 4 grams of sodium chloride and 1 gram of dried sodium carbonate added. The solution was then covered with kerosene (about 10 drops) to prevent frothing, the cylinders were corked, and the cylinder and acid bottle connected to the pump and aspirated for 4 hours. The acid was then washed down in the receiving bottle and the solution titrated with tenth-normal sodium hydroxide.

To calculate the amount of ammonia present, the number of cubic centimeters of tenth-normal sulphuric acid was multiplied by the tenth-normal sulphuric acid factor, and from this was subtracted the number of cubic centimeters of alkali used in titration. This result multiplied by 0.0017 and then by one one-hundredth of the total 24-hour urine gave the amount of ammonia.

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[1] Benedict, Journ. Am. Chem. Soc., 1900, **22**, pp. 259–263.
[2] Folin, Zeit. f. physiol. Chem., 1902, **37**, pp. 161-176.

DETERMINATION OF DIACETIC ACID.

The diacetic acid was determined qualitatively by the addition of an aqueous solution of chloride of iron to the urine (Gerhardt's reaction). The intensity of the ferric chloride reaction was recorded by the following symbols: +, + +, + + +, + + + +.

The tables furnish some information upon the value of Gerhardt's test in the determination of diacetic acid and its importance in estimating the total acidosis, or more correctly, the large per cent of the total acidosis as represented by β-oxybutyric acid. The lowest and highest quantities of β-oxybutyric acid present upon the days the diacetic acid was estimated and the intensity of the diacetic acid reaction upon these days are given in table 4.

TABLE 4.—*Comparison of diacetic acid and β-oxybutyric acid.*

Diacetic acid.	β-oxybutyric acid.
symbol.	*grams.*
0	5.7 to 11.0
+	7.0 14.2
+ +	8.5 55.3
+ + +	13.3 51.0
+ + + +	17.6 36.8

It is evident from these results that large quantities of β-oxybutyric acid may be present in the urine even though the ferric chloride reaction for diacetic acid is absent. Almost the maximum quantity of β-oxybutyric acid obtained in any of the cases was found in a urine in which the ferric chloride reaction was recorded as only + +. The reaction, however, certainly does possess some value, but as soon as it is strongly positive, as shown by + +, no idea can be formed as to whether the quantity of β-oxybutyric acid is in the neighborhood of 8 grams or 55 grams.[2]

DETERMINATION OF B-OXYBUTYRIC ACID.

The method employed for making this determination is that used in the laboratory of Professor Otto Folin and described by Black,[1] and involves the drying of a definite amount of urine to a small volume with an alkali. Subsequently acid is added and the water taken up by mixing with plaster of paris. The β-oxybutyric acid is extracted with ether and the rotation measured. The practical application of this method, as carried out in the laboratory, is as follows:

100 c. c. of urine are measured with a pipette into an evaporating dish and made distinctly alkaline by the addition of sodium bicarbonate. The urine is then evaporated to a thick syrupy liquid (4 or 5 c. c.) using the gentle heat of the water bath or the low heat of an electric stove. After cooling, the residue is made distinctly acid with strong hydrochloric acid and is then formed into a thick paste and later into a porous meal by the gradual addition of plaster of paris.

[1] Black, Journ. Biol. Chem., 1908, **5**, p. 207.

[2] See p. 72 for further discussion.

This porous meal is placed in an extracting apparatus (a Soxhlet or a modification of it) and extracted with about 60 c. c. of ether for 3 hours. The ether extract is then transferred to an evaporating dish where the ether is allowed to evaporate spontaneously. The residue is treated with 5 c. c. of water and 0.4 gram of boneblack added to decolorize, then filtered and washed until perfectly clear and made up to a known volume, usually 25 c. c. The β-oxybutyric acid is determined with a polariscope, using the following formula:

$$\frac{\text{Angle observed.}}{\text{Specific rotation of } \beta\text{-oxybutyric acid (24.12)} \times \text{length of polarizing tube (200 m. m.)}} = \text{Grams of } \beta\text{-oxybutyric acid in 1 c. c.}$$

Estimations of the quantity of β-oxybutyric acid based on the difference between the 24-hour quantity of sugar obtained by polarization and by Citron's method are known to be inaccurate. They must be erroneous, as 1 gram of sugar by rotation does not equal 1 gram of β-oxybutyric acid by rotation, since each body has a different specific rotary power. Our tables throw light upon the extent of the error, because we can compare such figures with the actual quantity of β-oxybutyric acid present as extracted by the Black method. As a rule the difference between the extracted quantity of β-oxybutyric acid and that estimated by the difference between the two tests for sugar did not exceed 5 or 10 grams, the acid obtained by extraction almost invariably exceeding that estimated by the difference of the sugar tests. It is true that the method of estimating the β-oxybutyric acid by difference is absolutely useless for quantitative work, but on the other hand it is equally certain that it is helpful clinically.

DETERMINATION OF SUGAR IN 1-HOUR PERIODS.

The determinations of the sugar in the urine reported in the statistics were made by the method of Citron, introduced in this laboratory by Dr. Falta of von Noorden's clinic in Vienna. The original description of the method was published by Citron in 1904,[1] and recently he has published a modified form of the method and discussed in detail the apparatus which he has devised for its use in clinical examinations.[2] The method depends upon the fact that the unreduced copper in the Fehling solution after boiling with urine reacts with potassium iodide in a sulphuric acid solution to liberate iodine. The amount of iodine liberated is determined by means of a standard solution of sodium thiosulphate, using starch paste as an indicator.

The following solutions are required for the carrying out of the method:

A copper solution, which is prepared by dissolving 692.7 grams of crystallized copper sulphate in water, making up the solution to 10 liters; an alkaline solution, prepared by dissolving 3460 grams of Rochelle salts and 2500 grams of potassium hydroxide (in stick form) in sufficient water to make 10 liters; a sodium thiosulphate solution, prepared by dissolving 250 grams of crystallized

[1] Citron, Deutsch. med. Wochenschrift, 1904, **30**, pp. 1602-1605.
[2] Citron, Deutsch. med. Wochenschrift, 1909, **35**, pp. 1189-1191.

sodium thiosulphate in sufficient water to make 10 liters; a potassium iodide solution, made by dissolving 200 grams of the salt in water to make 1 liter; and finally a 25 per cent solution of sulphuric acid.

The process of the determination of sugar in urine is carried out as follows: Exactly 10 c. c. of the copper sulphate solution are delivered into an Erlenmeyer flask of 300 to 500 c. c. capacity and 10 c. c. of the alkaline Fehling solution added. The flask and contents are thoroughly shaken in order to prevent the formation of insoluble copper oxide. About 80 c. c. of distilled water are then added and the flask and contents placed over a flame. When the solution boils, 1 or 2 c. c. of urine, according to its concentration, are added and the solution allowed to boil exactly 2 minutes. The flask is next removed from the flame and 20 c. c. of the 25 per cent sulphuric acid solution are added and then 20 c. c. of the potassium iodide solution. The solution is thoroughly shaken and the starch paste added, and while still hot, the sodium thiosulphate solution is rapidly added until the blue color disappears and the precipitate is nearly white.

Standardization and calculation.—When the solutions are properly prepared, it is found that the iodine liberated by means of the 10 c. c. of alkaline copper sulphate solution will combine with 27.8 c. c. of sodium thiosulphate solution. In practice it has been found that the sodium thiosulphate solution does not

TABLE 5.—*Citron sugar test.*

	mg. dextrose.		mg. dextrose.		mg. dextrose.
1 c. c. =	3.1	10 c. c. =	32.3	19 c. c. =	63.3
2	6.1	11	35.7	20	66.6
3	9.3	12	39.1	21	70.7
4	12.5	13	42.5	22	74.5
5	15.7	14	45.9	23	78.5
6	19.0	15	49.3	24	82.5
7	22.3	16	52.8	25	86.5
8	25.6	17	56.3	26	90.6
9	28.9	18	59.8	27	94.8

always when first made up correspond to the 10 c. c. of copper sulphate solution, and it is necessary to adjust the solution to meet this requirement. Based upon this blank, so called, table 5 has been prepared, from which the number of milligrams of dextrose can be computed corresponding to the different amounts of sodium thiosulphate computed by subtracting that combining with the free iodine from 27.8 c. c. The table is given herewith. For example, since the amount of thiosulphate solution added after the sugar in the sample of urine reduced a portion of the copper sulphate was 10 c. c., then, obviously, sufficient copper had been reduced to correspond to 17.8 c. c. of thiosulphate, and 17 c. c. of thiosulphate corresponds, according to table 5, to 56.3 milligrams of dextrose and 0.8 c. c. to 2.56 milligrams, so that the results would be $56.3 + 2.56 = 58.8$ milligrams of dextrose. In order to standardize the method, it is best to use a dextrose solution containing 15 grams of dextrose to 1 liter of solution, and from this amounts varying from 1 to 5 c. c. are used and the accuracy of the method thus determined. It is frequently found that it is necessary to correct the results

obtained as much as 3 to 4 per cent. All of the work done with this method is based upon the standardization with the dextrose solution.

The method permits of rapid determinations, but has not as high a degree of accuracy as is desirable in accurate scientific work. It is an empirical one and must be followed very exactly. It has been found, for instance, that any diminution of the amount of acid used makes the end point very difficult to determine, although the amount stated is very much in excess of that required to neutralize the alkali in the solution.

DETERMINATION OF SUGAR IN 24-HOUR PERIODS.

The estimations of sugar as recorded upon the clinical chart were made with a polariscope of standard make. They, therefore, are accurate, except in the presence of levo-rotary bodies. As the majority of the cases presented acidosis, and so have β-oxybutyric acid in the urine, the polariscopic readings for sugar can usually be considered low. Frequently, sugar was also determined by the Citron method, and this is recorded on the clinical charts, but this method as applied in a private laboratory was not as accurate as when it was carried out with almost daily control tests in the Nutrition Laboratory. However, frequent comparative tests were made to insure the reliability.

Looking over the literature of diabetes and case reports, it is interesting to note that frequently the per cent and quantity of sugar, as determined by Fehling's solution, is less than that determined by the polariscope even when levo-rotary bodies are present. Such figures almost always represent errors. We are inclined to doubt the reliability of the quantity of sugar determined by Fehling's or even the Citron method, unless special precautions are taken to secure its accuracy—precautions that are not easily carried out in private laboratories. Furthermore, in all cases, analyses must be promptly performed as a loss in reducing power rapidly takes place.

PART II.

STATISTICS OF EXPERIMENTS ON METABOLISM IN DIABETES.

Recognizing the difficulty of comparing normal people with diabetics, it was deemed advisable to make the investigation so extensive and to include so many different individuals that broad generalizations could be drawn, thus eliminating the personal equation in so far as possible. Consequently thirteen different subjects were used in the investigation. These thirteen individuals were all private patients, which accounted for the readiness with which they underwent the various experiments. With two exceptions, they took a deep interest in the work, although they realized that the immediate results could only indirectly benefit them personally. Eleven of the patients spent one or more weeks at the New England Deaconess Hospital. The habits of the patients were correct as to alcohol and tobacco, and no suspicion of lues arose in any one case.

Classification of Cases.

The cases have been divided into three groups—severe, moderately severe, and mild diabetes.

Group I.—Severe diabetes, 10 cases (A to J, inclusive). This group includes all cases who failed to become sugar-free even though all carbohydrates except the green vegetables were excluded from the diet, or those who became temporarily sugar-free upon vegetable days, which were preceded and followed by a low quantity of protein in the diet. The cases in this group invariably showed a minus carbohydrate balance, when the diet was considerably restricted. The second criterion for determining the severity of a case was the presence of acidosis. This existed in all cases of this group, and usually to a marked degree.

Group II.—Moderately severe diabetes, two cases (K and L). The basis for grouping is first, that the patients became sugar-free and showed a positive carbohydrate balance, and second, that the acidosis was either very slight or absent.

Group III.—Mild diabetes, one case (M). This was a fat man who was able to assimilate at least 100 grams of carbohydrate per day.

This classification and a brief description of the cases are given in table 6.

Diet.

The diet of the patients while under observation was fairly constant. Of the 13 cases studied, 11 of the subjects spent several days or weeks at either the New England Deaconess or the Corey Hill hospitals, where the nurses are thoroughly accustomed to diabetic patients, and the diabetic diet and the use of diabetic charts are a matter of routine. Each meal was recorded on the chart.

TABLE 6.—*Classification and description of cases used in the studies on diabetes.*

Group number and description of case.	Designation of case.	Sex.	Age at onset.	Onset.	Condition April, 1910.	Duration up to April, 1910.
Group I (severe).	A	M.	39	Gradual, 1900..	Fair health....	10 + y.
	B	F.	39	Gradual, Dec., 1908.	Light work [1]...	1 y. 4 mo.
	C	M.	28	Acute, Sept., 1908.	Died, coma, Dec. 8, 1909...	15 mo.
	D	M.	31	Mar., 1909.....	Died, coma, Jan. 13, 1910..	10 mo.
	E	M.	17	Sept., 1907.....	Died, coma, Oct. 13, 1909..	2 y. 1 mo.
	F	M.	22	Jan., 1908.....	Died, pneumonia, Feb., 1910.	2 y. 1 mo.
	G	M.	31	Transitory glycosuria, Jan., 1901; final onset, Jan., 1905.	Marked debility.[1]	5 y. 3 + mo.
	H	F.	17	1889	Active work [1]..	21 + y.
	I	M.	13	1900	Light work...	10 + y.
	J	M.	21	Feb., 1908.....	Comfortable ..	2 + y.
Group II (moderate).	K	M.	44	Nov., 1907.....	Active work...	2 y. 5 + mo.
	L	M.	21	July, 1908.....	Active work...	1 y. 9 + mo.
Group III (mild).	M	M.	47	1900	Active work...	10 + y.

[1] B, G, and H also died in coma, May, 1910.

The carbohydrates of the diet were given in the form of bread, oatmeal, potato, milk, cream, oranges, grape fruit, and vegetables. The percentage of carbohydrate in each article was estimated upon the following basis:

Food material.	Carbohydrate.
Bread ....per cent..	60
Oatmeal (uncooked).......do....	66
Potato (cooked)...........do....	20
Milk ....do....	5
Cream ....do....	2.5
1 orange ....grams..	10
One-half grape fruit........do....	5

The vegetables used were lettuce, spinach, cabbage, cauliflower, string beans, celery, asparagus, cucumbers, egg plant, rhubarb, tomatoes, and onions. 300 grams of vegetables was the amount daily given, and this amount was considered to contain 10 grams of carbohydrates.

The protein was given in the form of eggs, meat, fish, cheese, bread, oatmeal, milk, and cream. It was estimated upon the following basis:

Food material.	Quantity.	Protein.	Nitrogen
	grams.	*grams.*	*grams.*
Meat, uncooked..........................	30	6.25	1
Cheese	90	25.00	4
Egg	1	6.25	1
Milk (1 qt.)............................	960 c. c.	30.00	5

The meat was weighed uncooked except in the case of chicken, which constituted but a small fraction of the meat taken. Fish was rarely given. The estimation of the nitrogen in the diet was only approximate, but that it was not far from correct was shown by direct analysis. The ~~protein~~ in the diet of one day was considered to be 17 grams. By direct analysis it was found to be 16 grams. nitrogen

The fat was given in the form of butter, cheese, oil, eggs, and bacon. The amount consumed was only approximately determined, but it certainly was in excess of that recorded, because the butter, milk, cream, cheese, oil, and eggs which were allowed were always eaten, and besides the food materials mentioned more or less bacon was taken.

The alcohol given in these experiments was either in the form of whiskey or brandy, in which it was assumed that 50 per cent of alcohol was present, or in the form of Zeltinger wine, which has no sugar but contains 10 per cent of alcohol.

TREATMENT.

Treatment consisted almost entirely in rearrangement of the diet. As soon as the patients came under observation they were put upon a diet including, approximately, 100 to 150 grams of carbohydrate. In two instances a larger quantity was given, because the disease had extended over many years, and it was felt unwise to make radical restrictions of diet so suddenly. In all cases the diet was gradually reduced, in most to a point at which only vegetables were given, so that the quantity of carbohydrate ingested during one day fell to 10 grams. Care was taken to insure an adequate amount of fat in the diet. No such need was met in the case of protein. On the other hand the amount was usually restricted to about 75 grams to 100 grams of protein a day.

The digestion of the patients improved as a rule when they were put upon a diet low in carbohydrates and rich in fat. This was striking with Case B, a frail woman, who entered the hospital with marked indigestion, but after three or four days was able to live upon a far more rigid diet than many patients can bear. On the other hand, Case L developed jaundice when he was put upon a diet somewhat richer in fats than the one to which he had been accustomed.

The carbohydrate balance (the difference between carbohydrate in the diet and carbohydrate in the urine) in these cases is necessarily only approximate, but nevertheless will be found to be of considerable value. Falta has called attention to the fact that the carbohydrate balance is a nearly constant quantity, so that any variations in it suggest dietetic or analytical errors. To a considerable extent we can substantiate this conclusion. Exceptions occur upon oatmeal days and also at such times in the course of treatment when the carbohydrate in the diet is suddenly greatly reduced. Under these circumstances a minus carbohydrate balance of a few grams may change to a positive carbohydrate balance of over 100 grams. At first we were inclined to believe that such a sudden change in the carbohydrate balance represented deceit on the part of the patient, but the results of oatmeal days conducted when the patients were under close supervision showed that such a change is perfectly possible.

Clinically there was no question in our minds but that Cases A, B, G, H, and I did better when the quantity of carbohydrate in the food reached as much as 75 grams. At that point, too, they were in better condition than they were when coming under treatment, with the quantity of carbohydrates in the diet far in excess of this amount. This appeared to be the happy mean for these special cases. There is no question regarding the advisability of total exclusion of carbohydrates from the diet to get the urine of the patient free from sugar, provided that when once sugar-free a positive carbohydrate balance can be built up. For example, a child 13 years old in March, 1908, had 55 grams of sugar in the urine with 90 grams of carbohydrates in the diet. The same child, now, in April, 1910, has no sugar in the urine and 60 grams of carbohydrate in the diet, but this only became possible under weeks of a carefully restricted diet.

Vegetable days were frequently used as a means of rendering the patient sugar-free. As a rule the plan was effectual, but this did not invariably occur with one vegetable day, and in some instances only with two vegetable days when these were preceded by a low protein diet. The vegetable days afforded a good means of estimating the progress of the disease, and this point will be noted under the respective cases. Oatmeal days were used in five of the cases while under observation. As a rule the oatmeal was borne well, but occasionally the quantity given was considerably below that prescribed by von Noorden. One patient, Case H, was unable to take large quantities of oatmeal so that no satisfactory test with this case was made. The results are given in table 7.

TABLE 7.—*Oatmeal, bread, and potato days.*

Case.	Date.	Food material.	Carbohydrates.	Preceding day.		Experimental day.		Following day.	
				Carbohydrate balance.	Acidosis.[1]	Carbohydrate balance.	Acidosis.[1]	Carbohydrate balance.	Acidosis.[1]
			gms.	*gms.*		*gms.*		*gms.*	
A	Dec. 13–14..	Oatmeal .	160	—10	+ + + +	+ 70	+ +	—15	+ +
	Jan. 14–15..	Bread ...	130	....	+ + +	— 10	+ + + +	....	....
	Jan. 18–19..	...Do.	130	....	+ + + +	— 10	+ + + +	....	....
	Jan. 31–Feb. 1..	...Do.	130	....	+ + + 3.4 gms.[3]	— 30	+ + + 2.9 gms.[3]	....	....
I	Nov. 5– 6..	Oatmeal .	90	—120	+	— 45	+ +	....	....
	Nov. 6– 7[2].	....	....	....	....	....	....	....	....
D	Nov. 3– 4..	Oatmeal .	200	....	....	+120	....	—40	....
C	Aug. 4– 5..	Oatmeal .	40	....	....	— 65	+ + + 18.5 gms.[4]	....	....
	Aug. 5– 6..	...Do.	100	....	....	+ 5	+ + 18.5 gms.[4]	....	....
	Oct. 26–27..	Potato ..	98	—55	29	— 10	33.6[4]	—70	61.0
	Oct. 29–30..	Oatmeal .	125	—40	61	+ 25	46.0[4]	—30	47.8
J	Oct. 12–13..	Oatmeal .	120	—15	+ + + +	+ 80	+	....	....
	Oct. 13–14..	...Do.	180	....	....	+115	+	—10	+
	Oct. 17–18..	...Do.	180	—15	+ + +	+ 90	+ +	....	....
	Oct. 18–19..	...Do.	180	....	....	+120	+ +	—25	+ +

[1] Acidosis is expressed in terms of diacetic acid, ammonia, or β-oxybutyric acid, the diacetic acid being expressed by symbols as follows: 0, +, + +, + + +, + + + +.
[2] Experiment omitted because of possible error.
[3] Ammonia.
[4] β-oxybutyric acid.

From this table it will be seen that the effect upon the carbohydrate balance from the use of oatmeal was decidedly favorable. In another series of experi-

ments we should be inclined to use oatmeal days more. A study of the carbohydrate balance would indicate that the oatmeal was burned in the body. On the other hand, these oatmeal days, either from a study of their effect on acidosis or from the results of observation in the calorimeter, afford no support to the view that the carbohydrate of oatmeal is oxidized in the body. Longer respiration experiments alone will be able to settle this point.

Bread was apparently of no effect in the three experiments in which it was used in lowering the minus carbohydrate balance or in diminishing the acidosis. Potato had a distinctly favorable effect upon the carbohydrate balance, but the acidosis was greater on the potato day and the day following than on the preceding day.

Sodium bicarbonate was freely used. It was not administered invariably at the slightest sign of acidosis (because the patients were under extremely close supervision) but rather when it was seen that the acidosis was persisting or increasing in intensity. The quantities used were usually about 12 to 24 grams, but occasionally the upper and lower limits were exceeded. No other medicine was regularly employed, though occasionally strychnine sulphate was given, and once (Case A) diuretin.

Care was taken to restrict the quantity of exercise whenever the patients were upon a low diet. Constipation was usually present, and treated by simple measures, such as the use of enemata, or salts, or most commonly by pills of aloin, 0.01 g.; strychnine sulphate, 0.001 g., and extract of belladonna, 0.008 g., or extract cascara sagrada, 0.3 g., or podophyllin, 0.008 g.

GENERAL CLINICAL COMPARISON OF CASES.

Four of the 13 patients (Cases C, D, E, and F) have died at the time of writing (April, 1910). Three of these (Cases C, D, and E) died in coma.[1]

It would appear that Case C corresponded most closely with Naunyn's type of pure diabetes. His carbohydrate balance showed the extent of deficient assimilation of the various forms of carbohydrate food employed and the experiments in the respiration calorimeter confirmed this view. From this lack of assimilation of carbohydrates and from the extent of the acidosis, it was evident some weeks before the end that he could not live but a short time. The duration of life of Case C after contracting diabetes was 15 months. During the first 7 months the diet was very little restricted, and during the balance of the period he at no time became sugar-free despite vegetable days. On the other hand, he was most faithful to diet, and probably the quantity of carbohydrate ingested seldom exceeded 100 grams during the last 8 months of his life.

When one compares the length of life of Case C with that of Case E, the question arises as to whether it was wise to have restricted the carbohydrate diet in Case C to 50 grams or even 100 grams for as long a time as it was so restricted. The question forces itself upon us whether he would not have stood a better

[1] Cases B, G, and H died in May, 1910, all in coma; in other words seven of the ten severe cases have died and six of these in coma.

chance of acquiring a storage of glycogen in the body with a more liberal supply of carbohydrate in the diet, even though the quantity of sugar in the urine was larger than with a restricted supply. This is suggested all the more by observing the rapid change in the carbohydrate balance of Cases H and I, when the carbohydrates in the diet were restricted from an unlimited quantity to about 100 grams. The change from a positive carbohydrate balance to a minus carbohydrate balance in Case I was so great in the short time as to lead to a perhaps unfounded suspicion of deceit on the part of the patient.

Case E represents the usual course of a case of diabetes not under close supervision. The duration of life, 2 years and 1 month, corresponds with the average period of life for diabetic patients at this age.

Case F probably would have lived for a somewhat longer period had he not contracted pneumonia. It would appear that he followed restriction of diet rather more carefully than Case E, but yet a diet which was not as restricted as Case C, and possibly this was to his advantage. His life was shortened by pneumonia unaccompanied by coma.

Case D is a most valuable case for comparison with these men. Although diabetes developed in March, 1909, he did not come under observation until December of that year. Not only was the case absolutely untreated for this period, but by great misfortune he took pains to eat an abundance of carbohydrate, especially in the form of sugar, during October and November. The debility of the patient was extreme, and it would appear that diabetic marasmus was responsible to a considerable degree for his early death. Acidosis was apparently not severe a few weeks before the end, although the extent of it was not finally determined. It is possible that in his weakened condition he succumbed to a degree of acidosis which would not have affected a stronger individual.

Case A was a mild case of diabetes grown severe by years of neglect. When treatment was instituted, improvement at first was marked, but was interrupted by an attack of influenza. Undoubtedly at this time the diet was too restricted, for when the patient went to the country and increased the quantity of carbohydrates from 50 to 100 grams, there was no question as to his improvement. Whereas the patient was a mild case at first and by neglect became a severe case, it is not improbable that the type of disease may now change and that the disease will again become of moderate though perhaps not of light intensity.

Case B at the time of writing has made a marked improvement.[1] Two factors stand out prominently, first, that this patient does better with 50 to 75 grams of carbohydrate than with 25 grams of carbohydrate, and second, that the use of sodium bicarbonate is most helpful.

Case G is an example of the necessity of treatment of transitory glycosuria.[1] He conforms to the data recently collected by Barringer and Roper,[2] in which they show that the majority of cases of transitory glycosuria which are discovered when being examined for life insurance subsequently develop diabetes. The

[1] Died, May, 1910.
[2] Barringer and Roper, Am. Journ. Med. Sci., 1907, **133**, p. 842.

favorable course of this case since the final onset in January, 1905, is attributable to the careful dietetic management of his physician.[1] In many respects it is similar to the famous case, No. 121, which occurred in Naunyn's series and was described by Weintraud.

Cases H and I are in a group by themselves. The former developed diabetes at the age of 17 and worked actively up to the time of her death in May, 1910, 19 years later. The latter developed diabetes at the age of 13. He was married 8 years after the onset and at the time of writing, April, 1910, has a child some 8 months old. Nine years after the onset he took up the occupation of chauffeur. This is a particularly unfortunate occupation for a diabetic patient, because it involves mental strain and bodily exposure.

It is noteworthy that the factor common to these two cases was the hereditary tendency to diabetes in their families. This was marked, as will be seen by reference to their histories. This is often considered a bad prognostic factor, but it is very questionable whether such is the case. Such cases should be studied in a group by themselves because it is probable that the course of hereditary diabetes is different from the course of diabetes under other conditions, and what is good therapeutically for one group may be harmful for another.

PLAN AND DETAILS OF EXPERIMENTS.

With the respiration calorimeter 56 experiments were made with the 13 different subjects. These experiments covered 193 periods, the periods averaging 1 hour each. With the respiration apparatus, 26 respiration experiments were carried out, with 102 periods, these periods being usually of 15 minutes' duration. The conclusions drawn from this investigation, therefore, are based upon a large number of experiments, and although the physical condition, body activity, gravity of the disease, and individuality may vary considerably with the different individuals, nevertheless an average of the total results should give a reasonably accurate picture of the metabolism during severe diabetes.

From a practical standpoint it was found best to make most of the experiments in the chair calorimeter, as this apparatus was finished some time before the bed calorimeter and experimental researches with it had already been begun. Accordingly but comparatively few experiments were made with the bed calorimeter, the number being about one-third that made with the chair calorimeter. The respiration apparatus was likewise not brought to completion until some time after the bed calorimeter was finished, and consequently the respiration experiments made with this apparatus have been confined to relatively few subjects. However, the results obtained with all three forms of apparatus are of sufficient importance to warrant a careful consideration and extensive comparisons are made in a subsequent discussion.

In the presentation of the experimental data, the following order has been maintained: First, the respiration calorimeter experiments when the subject

[1] Dr. Theodore C. Janeway.

was without food; second, the respiration calorimeter experiments made with food; and, finally, the respiration experiments. Under these different heads, the experiments are arranged chronologically. In certain instances, a larger number of respiration experiments was made than of calorimeter experiments, and it may thus happen that the most recent experiment of all, namely, a calorimeter experiment, may first be presented in the statistical data, while subsequently respiration experiments, made several months prior, are reported. A list of the experiments is given in table 8.

TABLE 8.—*List of experiments with diabetics.*

Case.	Respiration-calorimeter experiments.						Experiments with respiration apparatus.	
	Chair calorimeter.				Bed calorimeter.			
	Without food.		With food.					
	No. of experiments.	No. of periods.	No. of experiments.	No. of periods.	No. of experiments.	No. of periods.	No. of experiments.	No. of periods.
A	[1] 9	32	[1] 7	22	1	5	..	..
B	..	..	..	..	1	3	4	17
C	8	25	2	6	1	2	14	56
D	..	..	..	..	..	..	3	12
E	2	6	2	6	..	..	..	..
F	1	3	1	3	..	..	..	..
G	..	..	2	8	1	5	..	..
H	..	..	..	..	5	13	1	3
I	2	5	..	..	..	..	..	..
J	1	3	..	..	..	..	3	9
K	1	4	..	..	..	..	1	5
L	4	21	..	..	1	6	..	..
M	2	7	..	..	1	3	..	..
Total.	30	106	14	45	11	37	26	102

[1] Experiment No. A 5 is included twice in this list, the first two periods as an experiment without food (A 5*a*) and the last two periods as an experiment with food (A 5*b*).

GROUP I. CASE A.

DESCRIPTION OF THE CASE.

Male; single; traveling salesman; developed diabetes in 1900 at the age of 39; came under observation in October, 1908.

Family history.—No history of diabetes in the family. Both father and mother died of angina pectoris, two sisters died in infancy, one sister is well.

Past history.—Mumps, measles, German measles, scarlet fever, influenza once or twice; very little alcohol used.

Present illness.—The disease first attracted attention by polydipsia and polyuria during 1900. It caused the patient little inconvenience; he underwent little dietetic treatment. In October, 1908, on account of a cold he was examined by a physician, and then for the first time began active treatment. Weakness was the principal symptom; the appetite was good but not excessive; constipation; sleep excellent; no headache, eyesight good.

Physical examination.—Height, 1.71 meters. Greatest weight, 68.2 kilograms; weight, October, 1908, 51.4 kilograms. Poor muscular development. Pale, coated tongue, teeth quite good. Pupils equal and react to light. Knee jerks absent, but they were later obtained in March, 1910. No edema. Lungs and heart normal. Somewhat later, temporarily, a systolic murmur was heard at the apex of the heart. Pulse, 96; blood-pressure, 165 m. m. (Riva Rocci). Liver extended 2 fingers' breadth below the costal margin. Spleen not felt.

General history of the case.—The patient was an excellent subject, and co-operated throughout all the experiments in the most obliging manner. At the time of the last observation, March 11, 1910, he was unquestionably in better condition than 2 years before, although the gain in weight was only 5 pounds. From October 29, 1908 until December 24, 1908, he was at the New England Deaconess Hospital, and under close supervision, but later he came to the laboratory from his home the morning of each experiment. Improvement was decided at the beginning of treatment, but the condition was stationary the latter part of November and December, 1908. Early in January, 1909, a severe cold with neuralgia and otitis media greatly weakened the patient, and he did not recover until he went away in the summer. The pulse increased in rate at this time. Improvement was marked in the summer, when the patient took about 100 grams of carbohydrate daily in contrast to about 50 grams at the hospital. The course of the disease is shown by the chart herewith (table 9).

Urine data.—The volume of urine varied from 865 c. c. to 4750 c. c. It was but little over 2000 c. c. while in the hospital, but rose to 3000 and even 4000 c. c. soon after leaving the institution in December, 1908. This was explained by a relaxation of the diet during a severe attack of influenza in January, 1909. The specific gravity varied from 1033 to 1014. Albumen at no time during the period of observation exceeded a very slight trace. The quantity of urinary nitrogen averaged 13.1 grams. This gives us one of the best controls of the patient's diet while he was away from the hospital. It is probably a safe inference that he seldom broke over the prescribed régime to any marked extent.

Sugar in urine.—The total quantity of sugar in the urine remained very constantly at about 75 grams, except when the diet was markedly changed, and similarly the carbohydrates in the diet were generally about 40 to 60 grams. The carbohydrate balance was thus about minus 40 to 60 grams. It exceeded plus 10 grams but once, and that was upon an oatmeal day, when it reached plus 70 grams to become minus the next day. Further, the days upon which the balance was positive (except the oatmeal day) the examination of the urine for sugar was only by the polariscope. The patient did not show a larger quantity of sugar in the urine when the first analysis was made because the diet was already somewhat restricted. Presumably the quantity of carbohydrates in the urine a few days before was considerably in excess of 94 grams. He became sugar-free but once, and then only after several vegetable days, and remained but a single day free from sugar.

TABLE 9.—*Clinical chart—Case A.*

Date.	Experiment No.	Volume of urine.	Specific gravity.	Reaction.	Diacetic acid.	β-oxybutyric acid.	Nitrogen.	Ammonia.		Sugar.	
								Total.	$\frac{NH_3 - N}{\text{Total N}}$	By Citron.	By rotation before fermentation.[1]
1908.		*c. c.*				*gms.*	*gms.*	*gms.*	*p. ct.*	*gms.*	*gms.*
Oct. 22–23......		3140	1025	....	+ +	....	....	...	....	..	94
Oct. 27–28......		3500	1025	ac.	Sl. +	....	....	...	....	..	98
Oct. 29–30......		....	....	....	+ +	....	....	...	....	..	[2]2.2
Oct. 30–31......		3075	1023	ac.	+ + +	....	....	...	....	77	74
Oct. 31–Nov. 1.		3120	1024	ac.	+	....	....	4.2	....	..	81
Nov. 1– 2......		2640	1024	ac.	Sl. +	....	14.2	3.6	20.9	86	84
Nov. 2– 3......		2430	....	ac.	+	....	15.1	3.5	19.1	82	73
Nov. 3– 4......		2475	1025	ac.	+	....	15.3	3.6	19.4	80	79
Nov. 4-5.....	**A 1**	**2260**	....	....	....	....	**14.47**	**3.3**	**18.8**	**67**	**59**
Nov. 5-6.....	**A 10**	**2165**	**1021**	ac.	+ + +	**13.3**	**14.51**	**3.0**	**17.0**	**74**	**52**
Nov. 6– 7......		2280	1021	ac.	+ + +	....	10.1	...	....	49.5	32
Nov. 7– 8......		2220	1023	ac.	+ + +	....	11.5	...	....	61	44
Nov. 8– 9......		2600	1023	ac.	+ +	....	12.66	2.6	16.9	69	57
Nov. 9–10......		2570	1024	ac.	+ +	....	12.91	...	....	66	51
Nov. 10–11......		3060	1023	ac.	+ + +	....	15.27	2.8	15.1	72	55
Nov. 11–12......		2600	....	....	....	....	12.98	...	....	64	42
Nov. 12–13......		2720	1023	ac.	+ +	....	14.09	...	....	66	44
} Nov. 13–14......		....	....	....	....	27	13.19	...	....	65	50
} Nov. 14–15......		5020	1022	ac.	+ + + +	27	13.19	...	....	65	50
Nov. 15–16......		2215	1026	alk.	+ + +	....	11.24	...	....	66	55
Nov. 16–17......		2230	1027	alk.	+ + + +	....	13.49	...	....	67	..
Nov. 17–18......		2305	1027	alk.	+ +	....	13.31	...	....	61	55
Nov. 18-19..	**A 2**	**1810**	....	....	....	....	**13.5**	**0.8**	**4.9**	**43**	**28**
Nov. 19-20..	**A 11**	**2450**	....	....	....	**4.2**	**17.4**	**0.9**	**4.3**	**71**	**67**
Nov. 20–21......		2120	1028	alk.	+ +	....	14.6	...	....	58	49
Nov. 21–22......		2115	1026	ac.	+ +	....	14.2	...	....	62	51
Nov. 22–23......		2050	....	....	....	....	13.0	...	....	77	71
Nov. 23-24..	**A 12**	**1970**	....	....	....	**0.6**	**12.4**	**0.5**	**3.3**	**78**	**69**
Nov. 24-25..	**A 13**	**2165**	....	....	....	**0**	**13.2**	...	....	**82**	..
Nov. 25–26......		2320	1024	ac.	+	....	....	...	....	..	46
Nov. 26–27......		....	....	....	....	....	....	...	....	..	..
Nov. 27–28......		2490	1019	ac.	0	....	....	...	....	..	45
Nov. 28–29......		1950	1023	alk.	Sl. +	....	....	...	....	..	51
Nov. 29–30......		2310	1024	alk.	+	....	....	...	....	..	35
Nov. 30–Dec. 1.		2250	....	alk.	+	....	....	...	....	..	41
Dec. 1– 2......		2550	1028	alk.	+	....	....	...	....	..	46

[1] All the determinations by rotation on this and all following charts were made before fermentation.
[2] Per cent.

TABLE 9.—*Clinical chart—Case A.*

Diet.									
Total carbohydrates.	Protein. N × 6.25.	Nitrogen.	Fat.	Alcohol.	Calories.	$NaHCO_3$.	Carbohydrate balance.[1]	Naked body-weight.	Remarks.
gms.	*gms.*	*gms.*	*gms.*	*gms.*		*gms.*	*gms.*	*kilos.*	
50	...	..	...	..	....	12	—45	51.3	
50	...	..	...	..	....	12	—50	50.8	
50	...	..	...	..	....	12	....	48.4	Previous weights late in day; from now on before breakfast.
40	...	..	...	18	....	12	—35	48.2	
55	106	17	180	33	2500	0	—25	48.1	4 eggs, 90 gms. cheese, 240 gms. meat (uncooked), 75 gms. bread, 300 gms. vegetables, 120 gms. butter, 15 gms. oil, 330 gms. wine.
55	106	17	180	33	2500	0	—30	47.7	Do.
55	106	17	180	33	2500	0	—25	48.1	Do.
55	106	17	180	33	2500	0	—25	48.6	Do.
35	**81**	**13**	...	**20**	....	**0**	**—30**	**49.0**	2 eggs, 45 gms. cheese, 240 gms. meat, 45 gms. bread, 300 gms. vegetables, butter, 15 gms. oil, 200 gms. wine.
35	**81**	**13**	...	**20**	....	**0**	**—40**	**48.6**	1 egg, 45 gms. cheese, 36 gms. oatmeal, 200 gms. wine, vegetables, butter, 30 gms. cream, 220 gms. cooked meat.
40	69	11	200	24	2400	20	—10	49.3	4 eggs, 90 gms. cheese, 36 gms. oatmeal, 300 gms. vegetables, 120 gms. butter, 250 c. c. cream, 240 gms. wine.
40	119	19	200	33	2700	20	—20	50.7	The same and 240 gms. meat. Wine, 330 gms.
40	119	19	200	33	2700	20	—30	51.5	4 eggs, 90 gms. cheese, 36 gms. oatmeal, 300 gms. vegetables, 120 gms. butter, 250 c. c. cream, 240 gms. wine.
40	119	19	200	33	2700	20	—25	52.4	Do.
40	119	19	200	33	2700	20	—30	53.3	Do.
25	113	18	200	33	2200	20	—40	53.3	The same save only 12 gms. oatmeal.
40	119	19	200	33	2700	20	—25	53.0	4 eggs, 90 gms. cheese, 240 gms. meat (uncooked), 36 gms. oatmeal, 300 gms. vegetables, 120 gms. butter, 250 c. c. cream, 240 gms. wine.
40	119	19	200	33	2700	20	—25	52.5	Do.
40	119	19	200	33	2700	20	—25	52.5	Do.
55	106	17	180	33	2500	20	—10	52.3	4 eggs, 90 gms. cheese, 240 gms. meat (uncooked), 75 gms. bread, 300 gms. vegetables, 120 gms. butter, 15 gms. oil, 330 gms. wine.
55	106	17	180	33	2500	20	—10	53.4	Do.
55	106	17	180	33	2500	20	— 5	52.7	Do.
35	..	**12**	...	**20**	....	**12**	**—10**	**52.9**	2 eggs, 45 gms. cheese, 210 gms. meat, 45 gms. bread, 300 gms. vegetables, butter, 15 gms. oil, 200 gms. wine.
55	..	**21**	...	**20**	....	**16**	**—15**	**52.9**	2 eggs, 45 gms. cheese, 240 gms. meat (uncooked), 75 gms. bread, 300 gms. vegetables, 237 gms. meat (cooked), butter, 15 gms. oil, 200 gms. wine.
55	..	17	180	33	2500	16	— 5	53.2	4 eggs, 90 gms. cheese, 240 gms. meat (uncooked), 75 gms. bread, 300 gms. vegetables, 120 gms. butter, 15 gms. oil, 330 gms. wine.
55	..	17	180	33	2500	16	— 5	53.4	Do.
80	..	17	180	33	2600	16	+ 5	53.7	The same and 25 gms. dextrose.
80	..	**17**	**180**	**33**	**2600**	**12**	**0**	**53.5**	4 eggs, 90 gms. cheese, 240 gms. meat (uncooked), 75 gms. bread, 300 gms. vegetables, 120 gms. butter, 15 gms. oil, 330 gms. wine.
80	..	**17**	**180**	**33**	**2600**	**12**	**0**	**53.7**	Do.
55	..	17	180	33	2500	12	+10	53.5	4 eggs, 90 gms. cheese, 240 gms. meat (uncooked), 75 gms. bread, 300 gms. vegetables, 120 gms. butter, 15 gms. oil, 330 gms. wine.
..	..	..	...	..	....	8	....	52.5	
55	..	17	200	33	2700	8	+10	52.2	The same and 30 gms. butter.
55	..	17	200	33	2700	12	+ 5	52.2	Do.
40	..	19	225	33	2900	20	+ 5	52.3	4 eggs, 90 gms. cheese, 240 gms. meat, 36 gms. oatmeal, 300 gms. vegetables, 150 gms. butter, 250 c. c. cream, 240 gms. wine.
40	..	17	225	33	2800	20	0	53.4	The same less 60 gms. meat.
40	..	17	225	33	2800	20	— 5	54.2	Do.

[1] When the sugar in the urine was not determined by the Citron method, the amount of sugar obtained by polarization was used in computing the carbohydrate balance.

TABLE 9.—*Clinical chart—Case A*—Continued.

Date.	Experiment No.	Volume of urine.	Specific gravity.	Reaction.	Diacetic acid.	β-oxybutyric acid.	Nitrogen.	Ammonia.		Sugar.	
								Total.	$\frac{NH_3 - N}{\text{Total N}}$	By Citron.	By rotation before fermentation.
1908.		*c. c.*				*gms.*	*gms.*	*gms.*	*p. ct.*	*gms.*	*gms.*
Dec. 2- 3......		2100	1028	alk.	+ + +	....	....	...	....	..	34
Dec. 3- 4......		1890	1027	alk.	+ + + +	....	....	...	....	37	19
Dec. 4- 5......		2290	1027	alk.	+ + + +	....	...	...	....	37	41
Dec. 5- 6......		2259	1028	alk.	+ + + +	....	....	...	....	41	36
Dec. 6- 7......		1770	1027	alk.	+ + + +	....	....	...	....	32	28
Dec. 7- 8......		2160	1025	alk.	+ + + +	....	....	...	....	32	35
Dec. 8- 9......		2040	1023	alk.	+ + + +	....	....	...	....	24	16
Dec. 9–10......		2520	1021	ac.	+ + + +	....	....	...	....	33	18
Dec. 10–11......		2730	1022	ac.	+ + +	....	....	...	....	46	27
Dec. 11–12......		2640	1026	ac.	+ + + +	....	....	...	....	..	26
Dec. 12–13......		2220	1026	ac.	+ + + +	....	....	...	....	38	18
Dec. 13–14......		2640	1025	Sl. ac.	+ +	....	....	...	....	92	90
Dec. 14–15......		2280	1023	alk.	+ +	....	....	...	....	23	18
Dec. 15–16......		1805	....	....	....	2.1	8.2	...	....	19	..
Dec. 16–17..	**A 3**	**865**	....	....	....	....	**5.93**	...	....	**8**	..
Dec. 17–18......		1140	1024	alk.	+ + +	....	....	...	....	Tr.	0
Dec. 18–19......		1680	1026	alk.	+ +	....	....	...	....	..	13
Dec. 19–20......		960	1033	Sl. ac.	+ +	....	....	...	....	..	13
Dec. 20–21......		1710	1027	alk.	Sl. +	....	....	...	....	17	14
Dec. 21–22......		2580	1014	ac.	T. Sl. +	....	....	...	....	..	15
Dec. 22–23......		2460	1018	ac.	+	....	....	1.7	....	..	30
Dec. 23–24......		2130	1023	ac.	+	....	....	...	....	..	38
1909.											
Jan. 4- 5......		3500	1027	ac.	+ + + +	....	....	4.3	....	132	..
Jan. 6- 7......		3500	1026	ac.	+ +	....	....	...	....	133	105
Jan. 7- 8......		3125	1027	ac.	+ + + +	....	....	...	....	116	94
Jan. 13–14......		4750	1023	ac.	+ + +	....	....	5.4	....	133	..
Jan. 14–15......		3500	1025	ac.	+ + + +	....	....	...	....	141	..
Jan. 17–18......		4250	1024	ac.	+ + + +	....	....	...	....	103	..
Jan. 18–19......		4000	1026	ac.	+ + + +	....	....	...	....	139	..
Jan. 24–25......		3500	....	....	+ + + +	....	....	...	....	44	..
Jan. 25–26......		3500	....	....	+ + +	....	....	...	....	137	..
Jan. 30–31......		3500	1028	ac.	+ + +	....	....	3.4	....	129	..
Jan. 31–Feb. 1.		3500	1030	ac.	+ + +	....	....	2.9	....	161	..
Feb. 8- 9......		4000	....	....	....	....	....	...	....	136	..
Feb. 12–13......		3500	....	....	+ +	....	....	...	....	85	..
Feb. 15–16......		3500	....	....	+ +	....	....	...	....	119	..
Feb. 22–23......		3500	1026	ac.	+ +	....	16.7	3.2	15.8	126	..
Mar. 1- 2......		3750	1029	ac.	+ +	....	....	...	....	150	..
Mar. 3- 4		4000	1026	ac.	+ +	35.6	14.2	4.1	23.8	128	..
Mar. 8- 9......		3500	1028	ac.	+ + +	....	....	...	....	130	105
Mar. 15–16......		4000	1023	ac.	+ + +	....	....	...	....	104	..
Mar. 18–19......		3610	1027	....	....	10.3	12.5	...	....	114	..
Mar. 29–30......		3250	1027	....	+ +	....	....	...	....	109	..
Apr. 1- 2......		2805	....	....	....	....	11.3	...	....	111	..
May 4- 5......		3070	1025	....	....	....	13.3	...	....	115	..
May 16–17......		2570	1026	....	....	....	11.9	...	....	102	..
June 7- 8......		2625	1027	ac.	+ +	....	....	...	....	87	89
Nov. 1- 2......		....	1024	ac.	+ + +	....	....	4.2	....	...	¹3
Nov. 4- 5......		3000	....	....	....	....	13.4	...	....	...	..
1910.											
Mar. 2- 3......		2565	1029	ac.	+	....	....	2.8	....	...	87
Mar. 5- 6......		2405	1024	ac.	+	16.6	11.7	3.0	21.1	79	67

¹ Per cent.

TABLE 9.—*Clinical chart—Case A*—Continued.

Diet.						$NaHCO_3$.	Carbohydrate-balance.	Naked body-weight.	Remarks.
Total carbohydrates.	Protein. N × 6.25.	Nitrogen.	Fat.	Alcohol.	Calories.				
gms.	*gms.*	*gms.*	*gms.*	*gms.*		*gms.*	*gms.*	*kilos.*	
16	..	16	225	33	2700	20	—20	54.8	Omit oatmeal.
16	..	16	225	33	2700	20	—20	55.8	Do.
40	..	14	225	33	2800	20	+ 5	56.3	4 eggs, 90 gms. cheese, 90 gms. meat, 36 gms. oatmeal, 300 gms. vegetables, 150 gms. butter, 15 gms. oil, 330 gms. wine.
40	..	14	225	33	2800	16	0	56.7	Do.
40	..	14	225	33	2800	16	—10	57.1	Do. Diuretin 2 gms.
40	..	14	225	33	2800	16	—10	57.8	Do.
10	..	..	...	..	....	16	—15	57.9	Yolks 14 eggs, bacon, 360 gms. wine, butter, vegetables, coffee, tea, bouillon.
30	75	12	240	36	2800	16	— 5	57.7	3 eggs, 90 gms. cheese, 90 gms. meat, 18 gms. oatmeal, 800 gms. vegetables, 150 gms. butter, 15 gms. oil, 250 gms. cream, 360 gms. wine.
30	75	12	240	36	2800	16	—15	57.4	Do.
30	75	12	240	36	2800	16	....	57.6	Do.
30	75	12	240	36	2800	16	—10	57.3	Do.
160	38	6	204	24	2800	12	+70	57.2	240 gms. oatmeal, 240 gms. butter, 240 gms. wine.
10	38	6	...	45	....	12	—15	56.8	Yolks 12 eggs, 300 gms. vegetables, bacon, butter, 450 gms. wine, bouillon, tea, coffee.
10	38	6	...	33	....	16	—10	57.2	The same except 330 gms. wine.
5	**13**	**2**	...	**12**	....	**4**	**— 5**	**56.5**	Bouillon, 1 egg, 2 egg-yolks, 90 gms. bacon, vegetables, 120 gms. wine, oil.
10	38	6	...	33	....	16	+10	56.5	As Dec. 15-16.
25	75	12	245	36	2900	16	+10	54.4	3 eggs, 90 gms. cheese, 90 gms. meat, 300 gms. vegetables, 150 gms. butter, 15 gms. oil, 250 c. c. cream, 360 c. c. wine, 1 grapefruit.
25	75	12	245	36	2900	20	+10	54.6	Do.
25	75	12	245	36	2900	4	+10	53.9	Do.
25	75	12	245	36	2900	0	+10	53.1	Do.
25	75	12	245	36	2900	0	— 5	52.3	Do.
25	75	12	245	36	2900	..	—15	51.7	Do.
...	..	..	...	..	....	..	....	....	
...	..	..	...	..	....	..	....	....	
...	..	..	...	..	....	..	....	....	
50	..	..	...	..	....	12	....	49.2	Meat, eggs, vegetables, 250 c. c. cream, 36 gms. oatmeal, 1 orange.
130	28	4.5	230	..	2700	12	—10	....	210 gms. bread, 250 c. c. cream, 210 gms. butter.
...	..	..	...	..	....	28	....	....	
130	28	4.5	200	..	2400	24	—10	49.9	210 gms. bread, 180 gms. butter, 250 gms. cream.
...	..	..	...	..	....	20	....	....	
130	28	4.5	200	..	2400	20	— 5	....	Do.
50	..	..	...	..	....	..	....	....	
130	28	4.5	200	..	2400	..	—30	....	Do.
70	..	..	...	..	....	..	....	....	
15	..	..	...	..	....	24	....	....	Vegetables, 250 c. c. cream, bouillon, butter, eggs, bacon, wine, coffee, tea.
60	..	..	...	..	....	16	....	50.7	36 gms. oatmeal, 250 c. c. cream, 2 oranges, vegetables, meat, eggs, wine.
60	..	..	...	..	....	16	....	....	Do.
60	..	..	...	..	....	16	....	51.5	
60	..	..	...	..	....	16	....	....	Do.
60	..	..	...	..	....	16	....	51.3	Do.
60	..	..	...	..	....	..	....	....	
..	..	..	...	..	....	..	....	....	
75	..	..	...	..	....	..	....	52.2	
..	..	..	...	..	....	..	....	....	
..	..	..	...	..	....	12	....	....	
..	..	..	...	..	....	..	....	....	
..	..	..	...	..	....	..	....	....	
..	..	..	...	..	....	16	....	53.7	
..	..	..	...	..	....	..	....	....	
60	..	..	...	..	....	8	....	53.6	36 gms. oatmeal, 250 c. c. cream, 1½ orange, ½ grapefruit, vegetables, meat, eggs, fat.
60	..	..	...	..	....	8	—20	....	

Quantitative indications in the urine of acidosis.—The acidosis was consistent with the minus carbohydrate balance, and the quantitative indications are shown in table 10. It was measured first by the intensity of the diacetic acid reaction. The diacetic acid was estimated by the depth of the color when an aqueous solution of ferric chloride was added to the urine. It varied from one plus (+) to four plus (+ + + +), being nearly always less severe when the patient was outside of the hospital, and presumably taking rather more carbohydrates in the diet.

TABLE 10.—*Quantitative indications in the urine of acidosis—Case A.*

Date.	Diacetic acid.[1]	β-oxy-butyric acid.	Ammonia. Total.	Ammonia. Per cent of total nitrogen.	Sugar. Citron method.	Sugar. Rotation.	Sugar. Difference (+ or —).
		gms.	*gms.*		*gms.*	*gms.*	*gms.*
Oct. 30–31	+ + +	....	3.3	....	77	74	— 3
Oct. 31–Nov. 1	+	....	4.2	....	..	81	..
Nov. 1– 2	sl. +	....	3.6	20.9	86	84	— 2
Nov. 2– 3	+	....	3.5	19.1	82	73	— 9
Nov. 3– 4	+	....	3.6	19.4	80	79	— 1
Nov. 4– 5	....	....	3.3	18.8	67	59	— 8
Nov. 5– 6	+ + +	13.3	3.0	17.0	74	52	—22
Nov. 8– 9	+ +	....	2.6	16.9	69	57	—12
Nov. 10–11	+ + +	....	2.8	15.1	72	55	—17
Nov. 13–14	....	[2]27	...	....	[2]65	[2]50	—15
Nov. 14–15	+ + + +	[2]27	...	....	[2]65	[2]50	—15
Nov. 18–19	....	....	0.8	4.9	43	28	—15
Nov. 19–20	....	4.2	0.9	4.3	71	67	— 4
Nov. 23–24	....	0.6	0.5	3.3	78	69	— 9
Nov. 24–25	....	....	...	....	82	..	..
Dec. 15–16	....	2.1	...	....	19	..	..
Dec. 22–23	+	....	1.7	....	..	30	..
1909.							
Jan. 4– 5	+ + + +	....	4.3	....	132	..	..
Jan. 13–14	+ + +	....	5.4	....	133	..	..
Jan. 30–31	+ + +	....	3.4	....	129	..	..
Jan. 31–Feb. 1	+ + +	....	2.9	....	161	..	..
Feb. 22–23	+ +	....	3.2	15.8	126	..	..
Mar. 3– 4	+ +	35.6	4.1	23.8	128	..	..
Mar. 18–19	....	10.3	...	....	114	..	..
June 7– 8	+ +	....	4.2	....	87	89	+ 2
1910.							
Mar. 2–3	+	....	2.8	....	..	87	..
Mar. 5–6	+	....	3.0	21.1	79	67	—12

[1] Intensity of reaction recorded: 0, +, + +, + + +, + + + +.
[2] Urine for 2 days combined and analyzed.

β-oxybutyric acid furnished the second source of information. The β-oxybutyric acid amounted to 13.3 grams upon November 5–6, 1908, when the patient was taking 35 grams of carbohydrate per day and no sodium bicarbonate, but it was 27 grams on the average for 2 successive days, November 13–14 and 14–15, when the carbohydrate in the diet was 40 grams, and 20 grams sodium bicarbonate had been taken daily for 7 days. The β-oxybutyric acid fell to 4.2 grams on November 19–20. For several days prior to this date the urine had been alkaline, and presumably most of the acid had been washed out of the system by

the use of fairly large doses of sodium bicarbonate. The β-oxybutyric acid was less than a gram upon November 23–24, and only 2.1 grams December 15–16. Upon 1 day, March 3–4, 1909, the quantity reached 35.6 grams. This was at the time the patient had left the hospital, and after he had had influenza, as above recorded. The patient was in a very critical condition at this time. The quantity of β-oxybutyric acid March 5–6, 1910, was 16.6 grams. The large quantity of β-oxybutyric acid was also indicated by the difference in the quantity of sugar as determined by the polariscope and by Citron's test. The table shows the relation between the extracted quantity of β-oxybutyric acid and the difference in the estimations of sugar by the Citron method and by polarization. The average difference between the two tests for sugar was 9 grams, the greatest being 22 grams. This is not an accurate method of estimating the acid as Magnus-Levy long ago showed, but it is often helpful.

The third index of the acidosis was the ammonia, which varied from 0.5 gram to 5.4 grams in contrast to 0.5 gram which is the normal amount of ammonia in the urine. Evidently the ammonia excretion was dependent upon whether sodium bicarbonate was being administered. The ammonia-nitrogen nitrogen ratio varied between 3.3 per cent and 23.8 per cent, in general being parallel to the other methods of measuring acidosis.

Another method of expressing the acidosis is by the quantity of sodium bicarbonate which it is necessary to give to render the urine alkaline. Whereas 5 grams of sodium bicarbonate will usually render the urine of a healthy individual alkaline, patient A took 20 grams daily for 9 days to produce this result. The patient felt better for taking the alkali, and continued it of his own accord, when for a period of several months he saw no physician. As a rule, the amount taken was 8 to 16 grams. The change in weight of the patient was closely dependent upon the quantity of the alkali, for it rose from 48.6 kilograms, November 5-6, 1908, to 53.3 kilograms 5 days later, the fifth day of the administration of 20 grams of sodium bicarbonate.

EXPERIMENTS WITH CASE A.

With this subject 16 metabolism experiments were made, 15 with the chair calorimeter and 1 with the bed calorimeter. Of these, 9 were made in the morning, after a fast of 12 hours, no breakfast being taken before or during the experiment. Food was taken in the other 7 experiments. One experiment (A 5) differed from the others in that while begun under fasting conditions, food was ingested at the beginning of the third period. The experiment is therefore divided in the text and also in the comparison of the experiments with this subject. The first two periods are included in the experiments without food, while the last two periods are considered in the experiments with food. No respiration experiments were carried out with this subject. The vital statistics were as follows:

Age, 49 years; height, 171 centimeters; range in naked body-weight,[1] 48.8 to 57.3 kilograms.

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[1] This range applies only to days of experiments.

METABOLISM EXPERIMENT No. A 1.

Date, November 4, 1908. Naked body-weight, 48.8 kilograms.

This experiment was the first made with a diabetic in which the respiration calorimeter was used. The subject had followed a dietetic régime in the New England Deaconess Hospital for several days previous to the experiment, and came to the laboratory without breakfast. The experiment proper began at $7^h\ 58^m$ a. m., and continued for three 2-hour periods. No water was taken during this time. The pulse-rate was taken by the subject himself, and ranged from 77 to 83, but no body-temperatures were obtained. He was very quiet throughout the whole experiment, the only activity being that incidental to urinating and to telephoning at the end of each period. He showed no nervousness regarding the experiment and proved an ideal subject. In the last period he covered the lower part of his body with a shawl but did not feel cool previous to that period. Some lightheadedness was experienced as well as headache, and the subject stated that the headache continued throughout the afternoon following the experiment. The metabolism measurements and the data regarding pulse-rate are given in table 11, while the statistics of the urine are given in table 12.

TABLE 11.—*Measurements of metabolism—Metabolism experiment No. A 1.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.[1]
			Carbon dioxide eliminated.	Oxygen absorbed.				
November 4, 1908.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
$7^h 58^m$ a.m. to $9^h 58^m$ a.m..	39.5	42.1	167	244	43.2	0.68	152	[2]81
9 58 a.m. 11 58 a.m..	38.7	39.9	164	233	58.1	.71	132	80
11 58 a.m. 1 58 p.m..	38.6	39.9	164	233	41.4	.71	134	81
Total 6 hours [3]......	116.8	121.9	165	237	142.7	....	418	..

[1] Pulse by the subject.
[2] Average of 3 records from 9 a. m. to 10 a. m.
[3] Carbon dioxide per kilogram per minute, 3.38 c. c.; oxygen per kilogram per minute, 4.86 c. c.; heat eliminated per kilogram per hour, 1.43 calories.

TABLE 12.—*Statistics of urine—Metabolism experiment No. A 1.*

Date and period.	Quantity.	Total nitrogen.	Sugar.		D : N.
			Polarization.	Titration.	
November 4–5, 1908.	*grams.*	*grams.*	*grams.*	*grams.*	
7 a.m. to 8 a.m.	84.5	.51	2.2	2.4	4.71
8 a.m. 10 a.m.	186.1	1.08	4.8	5.3	4.91
10 a.m. 12 noon	169.7	1.04	4.2	4.9	4.71
12 noon 2 p.m.	118.3	.81	3.2	3.4	4.20
2 p.m. 7 a.m.	1700 c. c.	11.01	44.2	50.5	....

METABOLISM EXPERIMENT No. A 2.

Date, November 18, 1908. Naked body-weight, 52.8 kilograms.

As in the previous experiment, the subject came to the laboratory in the morning without breakfast. He entered the calorimeter chamber at 7^{h} 59^{m} a. m. and the experiment began at 8^{h} 52^{m} a. m., continuing for three 2-hour periods. The subject drank no water. He used the telephone at the end of each period and also at 11^{h} 12^{m} a. m. The pulse-rate, which ranged from 63 to 70, was recorded every half hour by the subject himself, and he also took his own body-temperature, sublingually, with a clinical thermometer, at the beginning of each period, and at the end of the experiment. In attempting to take his temperature at 10^{h} 52^{m} a. m. (the beginning of the second period) he broke the thermometer, and another one was substituted, so that the second temperature record was taken at 11^{h} 12^{m} a. m., instead of at the beginning of the second period. The subject did not find this experiment so tedious as the first one or feel the lack of food so much, and suffered from no headache. The measurements of the metabolism are given in table 13, together with the average pulse-rate. The statistics of the urine are given in table 14.

TABLE 13.—*Measurements of metabolism—Metabolism experiment No. A 2.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.				
November 18, 1908.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
8^{h} 52^{m} a.m. to 10^{h} 52^{m} a.m.	38.5	.....	163	....	47.9	....	137	69
10 52 a.m. 12 52 p.m.	37.8	38.0	160	222	46.3	0.72	134	67
12 52 p.m. 2 52 p.m.	37.9	40.5	161	236	45.8	.68	131	65
Total 6 hours[1]	114.2	[2]78.5	161	[2]229	140.0	....	[3]402	..

[1] Carbon dioxide per kilogram per minute, 3.05 c. c.; oxygen per kilogram per minute, 4.34 c. c.; heat eliminated per kilogram per hour, 1.27 calories.
[2] For period 10^{h} 52^{m} a. m. to 2^{h} 52^{m} p. m.
[3] Body-temperature at beginning 97.75° F.; at end, 97.35° F. Heat production for total 6 hours, 393 calories.

TABLE 14.—*Statistics of urine—Metabolism experiment No. A 2.*

Date and period.	Quantity.	Total nitrogen.	Sugar.		D : N.
			Polarization.	Titration.	
November 18–19, 1908.	*grams.*	*grams.*	*grams.*	*grams.*	
7^{h} 00^{m} a.m. to 8^{h} 52^{m} a.m.	102.2	0.80	3.9	3.9	4.88
8 52 a.m. 10 52 a.m.	97.9	.79	2.9	3.4	4.30
10 52 a.m. 12 52 p.m.	58.7	.55	1.3	1.6	2.91
12 52 p.m. 2 52 p.m.	50.2	.52	.6	1.0	1.92
2 52 p.m. 7 00 a.m.	1500 c. c.	10.87	19.5	33.5	....

METABOLISM EXPERIMENT No. A 3.

Date, December 16, 1908. Naked body-weight, 57.3 kilograms.

The subject entered the calorimeter chamber at $8^h 20^m$ a. m., without breakfast, and the experiment began at $9^h 18^m$ a. m. The measurements of the metabolism were made in six 1-hour periods. No water was taken in the experiment and the subject used the telephone eight times. The subject stated after the experiment that he was neither tired nor unusually hungry. He suffered some from indigestion, but this had no connection with the experiment.

The pulse and respiration records were obtained by means of the stethoscope, which was used in this experiment for the first time with this subject. Records of the pulse-rate were also made by the subject himself. The range with the stethoscope was from 64 to 67, while the records made by the subject ranged from 65 to 71. Measurements of the body-temperature were taken sublingually with a clinical thermometer at the beginning of each period and at the end of

TABLE 15.—*Measurements of metabolism—Metabolism experiment No. A 3.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.
December 16, 1908.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
$9^h 18^m$ a.m. to $10^h 18^m$ a.m.	22.3	21.5	189	251	26.3	0.76	77	66
10 18 a.m. 11 18 a.m.	22.0	21.6	187	252	27.2	.74	79	64
11 18 a.m. 12 18 p.m.	22.3	21.6	189	252	26.3	.76	77	66
12 18 p.m. 1 18 p.m.	21.0	21.3	178	249	25.7	.72	79	..
1 18 p.m. 2 18 p.m.	22.3	21.7	189	253	25.8	.75	69	[1]64
2 18 p.m. 3 18 p.m.	21.7	21.3	184	249	24.9	.74	73	[2]66
Total 6 hours [3]	131.6	129.0	186	251	156.2	....	[4]454	..

[1] Average of three records from $1^h 40^m$ p. m. to $1^h 55^m$ p. m.
[2] Records taken from $2^h 50^m$ p. m. to $3^h 10^m$ p. m.
[3] Carbon dioxide per kilogram per minute, 3.25 c. c.; oxygen per kilogram per minute, 4.38 c. c.; heat eliminated per kilogram per hour, 1.33 calories.
[4] Rectal body-temperature at beginning, 36.85° C.; at end, 37.04° C. Heat production for total 6 hours, 461.2 calories.

TABLE 16.—*Statistics of urine—Metabolism experiment No. A 3.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
December 15, 1908.	*c. c.*		*grams.*	*grams.*	
$7^h 00^m$ a.m. to $7^h 00^m$ p.m.	872	....	3.91	12.9	....
December 15–16.					
$7^h 00^m$ p.m. to $1^h 00^m$ a.m.	641	1.023	2.64	3.5	....
December 16.					
$1^h 00^m$ a.m. to $7^h 00^m$ a.m.	292	....	1.65	2.3	....
$7^h 00^m$ a.m. to $9^h 18^m$ a.m.	95	1.029	.56	1.9	3.39
9 18 a.m. 11 18 a.m.	83	1.027	.53	1.5	2.83
11 18 a.m. 1 18 p.m.	70	1.028	.50	1.2	2.40
1 18 p.m. 3 18 p.m.	49	1.027	.36	.4	1.11

the experiment. The rectal measurements were also taken with the electrical-resistance thermometer. The measurements of the metabolism and the average pulse-rate are given in table 15. The statistics regarding the urine are given in table 16.

METABOLISM EXPERIMENT NO. A 4.

Date, March 4, 1909. Naked body-weight, 51.6 kilograms.

The bed calorimeter was used for this experiment and the subject entered the chamber at $8^h\ 16^m$ a. m., without breakfast. The experiment began at $8^h\ 50^m$ a. m. and ended at $11^h\ 50^m$ a. m. The first period was 1 hour long and the four following, one-half hour each. During the experiment, the subject's body was three-quarters covered by a blanket. He used the telephone twice and turned over from one side to the other at $10^h\ 12^m$ a. m. and at $11^h\ 04^m$ a. m. The subject said that while there was sufficient light for reading, the position was not favorable, and although he did not sleep during the experiment, he was drowsy a part of the time. He also said that while he did not object to the bed calorimeter, he preferred the chair calorimeter, as the experiment seemed less tedious. The records of the pulse-rate were obtained with the stethoscope and ranged from 75 to 86, although at one time when the subject was moving about it rose to 91. The respiration-rate ranged from 12 to 18, and was obtained by means of the pneumograph, which was used in this experiment for the first time with this subject. The body-temperature measurements for the beginning of each period and at the end of the experiment were obtained with the electrical-resistance thermometer.

Certain interpretations of the metabolism may in large measure depend upon the variations in muscular activity, and an accurate record of the movements of the subject during the experiment may be obtained from the record of the vibrations of the tambour connected with the pneumograph. While the subject was instructed to lie quietly in the bed calorimeter there are frequently noticeable differences in the muscular activity with different individuals even under these

TABLE 17.—*Measurements of metabolism—Metabolism experiment No. A 4.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
March 4, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$8^h 50^m$ a.m. to $9^h 50^m$ a.m.	19.7	....	167	....	22.6	....	55	84	16
9 50 a.m. 10 20 a.m.	10.2	....	173	....	11.9	....	31	84	17
10 20 a.m. 10 50 a.m.	9.7	....	165	....	12.1	....	30	80	14
10 50 a.m. 11 20 a.m.	9.2	....	156	....	12.0	....	33	79	15
11 20 a.m. 11 50 a.m.	9.9	....	168	....	12.0	....	27	82	15
Total 3 hours [1].....	58.7	56.0	166	218	70.6	0.76	[2]176	..	..

[1] Carbon dioxide per kilogram per minute 3.22 c. c.; oxygen per kilogram per minute, 4.22 c. c.; heat eliminated per kilogram per hour, 1.14 calories.
[2] Rectal body-temperature at beginning, 36.30° C.; at end, 36.65° C. Heat production for total 3 hours, 192 calories.

conditions and, indeed, with the same individual during different periods. The subject was very quiet for the most of the experiment.

The metabolism measurements and the average pulse- and respiration-rates are given in table 17, and the statistics regarding the urine in table 18.

TABLE 18.—*Statistics of urine—Metabolism experiment No. A 4.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
March 4, 1909.	*c. c.*		*grams.*	*grams.*	
$7^h 00^m$ a.m. to $8^h 51^m$ a.m.	183	1.027	0.77	6.6	8.57
8 51 a.m. 10 21 a.m.	200	1.024	.74	5.6	7.57
10 21 a.m. 11 51 a.m.	155	1.023	.62	3.9	6.29

METABOLISM EXPERIMENT NO. A 5A.

Date, March 13, 1909. Naked body-weight, 51.4 kilograms.

The subject entered the calorimeter chamber at $8^h 07^m$ a. m. without breakfast and the experiment began at $9^h 02^m$ a. m. The measurements of the metabolism were in four 1-hour periods, but at the beginning of the third period the subject took food, and consequently the experiment will be considered in two parts, the first 2 hours as a fasting experiment, and the second as a food experiment—No. A 5*b*. The body-temperatures were obtained with the electrical-resistance thermometer, but during a part of the first period the thermometer was found to be displaced and accurate records were not obtained until the middle of the period. This also affected the calculation of the heat production. The pulse-rate as obtained with the stethoscope ranged from 85 to 94, and the respiration-rate supplied by the pneumograph, ranged from 17 to 20. The records of the metabolism measurements may be found in table 19, and the statistics regarding the urine in table 20.

TABLE 19.—*Measurements of metabolism—Metabolism experiment No. A 5.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
March 13, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$9^h 02^m$ a.m. to $10^h 02^m$ a.m.	21.1	21.0	179	245	21.6	.73	77	91	18
10 02 a.m. 11 02 a.m.	19.7	22.3	167	260	22.7	.64	77	89	19
11 02 a.m. 12 02 p.m.	21.3	20.3	181	237	22.4	.76	[1]72	88	18
12 02 p.m. 1 02 p.m.	21.7	21.3	184	249	22.9	.74	73	84	18
Total 4 hours [2].....	83.8	84.9	178	248	89.6	...	[3]299	..	..

[1] Not corrected for coffee taken during this period.

[2] Carbon dioxide per kilogram per minute, $9^h 02^m$ a. m. to $11^h 02^m$ a. m., 3.37 c. c.; $11^h 02^m$ a. m. to $1^h 02^m$ p. m., 3.56 c. c.; oxygen per kilogram per minute, $9^h 02^m$ a. m. to $11^h 02^m$ a. m., 4.92 c. c.; $11^h 02^m$ a. m. to $1^h 02^m$ p. m., 4.73 c. c.; heat eliminated per kilogram per hour, $9^h 02^m$ a. m. to $11^h 02^m$ a. m., 1.50 calories; $11^h 02^m$ a. m. to $1^h 02^m$ p. m., 1. 42 calories.

[3] Rectal body-temperature at beginning, 38.34° C.; at end, 38.84° C. Heat production for total 4 hours, 323 calories.

METABOLISM EXPERIMENT No. A 5B.

Date, March 13, 1909. Naked body-weight, 51.4 kilograms.

As previously stated, experiment A 5 was divided into two parts, the first two periods fasting, and the last two 1-hour periods with food. At the beginning of the third period of the experiment, the subject ate 25 grams of dextrose and 75 grams of white bread and drank a cup of cold coffee. He stated that he was quite hungry when he took the food. The body-temperature was measured with the electrical-resistance thermometer. The pulse-rate as obtained with the stethoscope ranged from 78 to 92, and the respiration-rate as given by the pneumograph ranged from 17 to 20. The metabolism measurements are given in table 19, and the statistics regarding the urine in table 20.

TABLE 20.—*Statistics of urine—Metabolism experiment No. A 5.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
March 13, 1909.	*c. c.*		*grams.*	*grams.*	
$7^h 00^m$ a.m. to $9^h 02^m$ a.m.	136	1.029	.69	5.7	8.26
9 02 a.m. 11 02 a.m.	136	1.028	.73	5.5	7.53
11 02 a.m. 1 02 p.m.	350	1.029	1.11	18.0	....

METABOLISM EXPERIMENT No. A 6.

Date, March 19, 1909. Naked body-weight, 51.4 kilograms.

The subject came to the laboratory without breakfast as in the experiments previously reported, but this experiment differed from those preceding in that he drank coffee twice while in the apparatus. Nearly all of the carbohydrates in the diet of the day preceding were eaten in the morning meal. He entered the chair calorimeter at $8^h 03^m$ a. m. and immediately afterward drank one cup of hot coffee. Neither milk nor sugar was used but the coffee was sweetened with saccharin. The experiment began at $8^h 47^m$ a. m. and continued for four 1-hour periods. At the beginning of the third period, the subject drank a cup of cold coffee, sweetened with saccharin. No water was taken during the experiment but the subject said that the cold coffee at the beginning of the third period prevented his feeling as hungry as in other fasting experiments. The pulse-rate, which was obtained by the stethoscope, ranged from 80 to 92, and the respiration-rate, obtained by means of the pneumograph, from 16 to 20. The body-temperature was measured by the electrical-resistance thermometer. The records for the last two periods were imperfect. A temperature measurement, taken sublingually after the subject left the calorimeter was 97.2° F.

The muscular activity during the experiment was slight. The subject telephoned twice, and at $11^h 47^m$ a. m. he adjusted the rectal thermometer, which was not recording accurately.

The measurements of the metabolism are given in table 21, and the statistics regarding the urine in table 22.

TABLE 21.—*Measurements of metabolism—Metabolism experiment No. A 6.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
March 19, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$8^h 47^m$ a.m. to $9^h 47^m$ a.m.	22.2	22.0	188	257	20.8	0.73	73	89	17
9 47 a.m. 10 47 a.m.	20.8	20.7	176	242	22.2	.73	74	87	18
10 47 a.m. 11 47 a.m.	21.6	22.2	183	259	22.6	.71	70	83	18
11 47 a.m. 12 47 p.m.	20.9	20.8	177	243	21.6	.73	75	83	19
Total 4 hours [1].....	85.5	85.7	181	250	87.2	....	[2]292	..	..

[1] Carbon dioxide per kilogram per minute, 3.52 c. c.; oxygen per kilogram per minute, 4.86 c. c.; heat eliminated per kilogram per hour, 1.42 calories.
[2] Rectal body-temperature at $8^h 47^m$ a. m., 36.13° C.; at $10^h 47^m$ a. m., 36.24° C. Heat production for period $8^h 47^m$ a. m. to $10^h 47^m$ a. m., 152 calories.

TABLE 22.—*Statistics of urine—Metabolism experiment No. A 6.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
March 18–19, 1909.	*c. c.*		*grams.*	*grams.*	
$7^h 00^m$ a.m. to $7^h 00^m$ p.m.......	1563	1.029	6.07	58.5	....
7 00 p.m. 7 00 a.m.......	2049	1.025	6.41	55.0	....
March 19, 1909.					
$7^h 00^m$ a.m. to $8^h 47^m$ a.m.......	169	1.027	.72	6.0	8.33
8 47 a.m. 10 47 a.m.......	320	1.023	1.08	8.0	7.41
10 47 a.m. 12 47 p.m.......	234	1.022	.89	5.1	5.73

METABOLISM EXPERIMENT NO. A 7.

Date, March 26, 1909. Naked body-weight, 52.2 kilograms.

The carbohydrates in the diet of the subject on the day preceding the experiment were for the most part taken in the last meal. The subject came to the laboratory in the morning without breakfast and entered the calorimeter chamber about $7^h 40^m$ a. m. As in the experiment previously reported, he drank immediately a cup of strong, hot coffee, without milk or sugar. The experiment began

TABLE 23.—*Measurements of metabolism—Metabolism experiment No. A 7.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
March 26, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$8^h 48^m$ a.m. to $9^h 48^m$ a.m.	19.4	20.1	165	235	24.1	0.70	70	87	16
9 48 a.m. 10 48 a.m.	19.7	20.2	167	236	24.7	.71	68	83	17
10 48 a.m. 11 48 a.m.	20.2	19.7	171	230	22.8	.75	71	80	17
11 48 a.m. 12 48 p.m.	19.6	20.7	166	242	22.6	.69	70	85	17
Total 4 hours [1].....	78.9	80.7	167	235	94.2	....	[2]279	..	..

[1] Carbon dioxide per kilogram per minute, 3.20 c. c.; oxygen per kilogram per minute, 4.50 c. c.; heat eliminated per kilogram per hour, 1.34 calories.
[2] Rectal body-temperature at beginning, 36.51° C.; at end, 36.79° C. Heat production for total 4 hours, 292 calories.

at $8^h 48^m$ a. m. and continued for four 1-hour periods. At the beginning of the third hour, he drank a cup of clear, cold coffee (137 grams). The pulse-rate, as indicated by the stethoscope, ranged from 77 to 90, and the respiration-rate, obtained by means of the pneumograph, ranged from 15 to 19. The body-temperature was measured with the electrical-resistance thermometer. The subject was fairly quiet throughout the experiment and made no comments regarding it. The muscular activity is shown by the pneumograph curve given in fig. 1. The hourly averages for the pulse- and respiration-rates, and the measurements of the metabolism are given in table 23 and the statistics for the urine in table 24.

TABLE 24.—*Statistics of urine—Metabolism experiment No. A 7.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
March 26, 1909.	*c. c.*		*grams.*	*grams.*	
$7^h 00^m$ a.m. to $9^h 50^m$ a.m.	251	1.025	1.06	8.7	8.21
9 50 a.m. 12 50 p.m.	284	1.024	1.27	7.0	5.51

METABOLISM EXPERIMENT NO. A 8.

Date, May 17, 1909. Naked body-weight, 49.5 kilograms.

In preparation for this experiment, it had been arranged that no meat or protein of any kind should be taken at the meal eaten the night preceding. This experiment was made with the chair calorimeter and the subject entered the chamber at $8^h 35^m$ a. m. without breakfast. The experiment began at $9^h 22^m$ a. m. and continued for four 1-hour periods. The stethoscope and pneumograph were used to obtain the records of the pulse- and respiration-rates, but the pneumograph failed to work properly after $10^h 44^m$ a. m. The pulse-rate ranged from 73 to 90, and the respiration-rate during the first 2 hours from 15 to 18. The body-temperature measurements were obtained by means of the electrical-resistance thermometer. The hourly averages for the pulse- and respiration-rates and the metabolism measurements are given in table 25, while the statistics for the urine are to be found in table 26.

TABLE 25.—*Measurements of metabolism—Metabolism experiment No. A 8.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
May 17, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$9^h 22^m$ a.m. to $10^h 22^m$ a.m.	20.4	26.9	173	314	29.5	....	71	85	16
10 22 a.m. 11 22 a.m.	19.3	18.6	164	217	28.2	0.75	69	78	[1]18
11 22 a.m. 12 22 p.m.	20.6	23.1	175	270	27.4	.65	72	83	..
12 22 p.m. 1 22 p.m.	19.8	19.2	168	224	26.0	.75	67	83	..
Total 4 hours [2].....	80.1	87.8	170	256	111.1	....	[3]279	..	...

[1] One record at $10^h 43^m$ a. m.
[2] Carbon dioxide per kilogram per minute, 3.43 c. c.; oxygen per kilogram per minute, 5.17 c. c.; heat eliminated per kilogram per hour, 1.41 calories.
[3] Rectal body-temperature at beginning, 36.95° C.; at end, 37.07° C. Heat production for total 4 hours, 285 calories.

TABLE 26.—*Statistics of urine—Metabolism experiment No. A 8.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
May 16–17, 1909.	*c. c.*		*grams.*	*grams.*	
$7^h 00^m$ a.m. to $7^h 00^m$ p.m.	1171	1.025	5.73	43.0	....
7 00 p.m. 7 00 a.m.	1398	1.026	6.18	58.6	....
May 17, 1909.					
$7^h 00^m$ a.m. to $9^h 26^m$ a.m.	146	1.027	.74	6.3	8.51
9 26 a.m. 11 26 a.m.	180	1.025	.86	6.0	6.98
11 26 a.m. 1 30 p.m.	105	1.026	.59	3.3	5.59

METABOLISM EXPERIMENT NO. A 9.

Date, November 5, 1909. Naked body-weight, 53.8 kilograms.

The subject entered the chair calorimeter, without breakfast, at $7^h 55^m$ a. m. The experiment began at 9 a. m. and continued for three 1-hour periods. No water was taken. The subject complained of a slight headache which was caused, he thought, by hunger. No other discomfort was felt during the experiment. The pulse- and respiration-rates were recorded by the stethoscope and pneumograph, the pulse-rate ranging from 67 to 77 and the respiration-rate from 14 to 16. The body-temperature measurements were obtained by means of the electrical-resistance thermometer. The subject was very quiet and fell asleep for a few minutes shortly after 11 o'clock. He used the telephone at the end of each period and also at $11^h 16^m$ a. m. The hourly averages of the pulse- and respiration-rates, and the measurements of the metabolism are given in table 27 herewith, and the statistics for the urine in table 28.

TABLE 27.—*Measurements of metabolism—Metabolism experiment No. A 9.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
November 5, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$9^h 00^m$ a.m. to $10^h 00^m$ a.m.	19.4	19.5	165	228	25.7	0.72	64	74	15
10 00 a.m. 11 00 a.m.	18.9	17.7	160	207	25.7	.78	61	69	15
11 00 a.m. 12 00 noon	19.5	19.9	165	232	26.0	.71	67	68	15
Total 3 hours [1]	57.8	57.1	163	222	77.4	....	[2]192	..	..

[1] Carbon dioxide per kilogram per minute, 3.03 c. c.; oxygen per kilogram per minute, 4.13 c. c.; heat eliminated per kilogram per hour, 1.19 calories.
[2] Rectal body-temperature at beginning, 36.52° C.; at end, 36.69° C. Heat production for total 3 hours, 200 calories.

TABLE 28.—*Statistics of urine—Metabolism experiment No. A 9.*

Date and period.	Volume.	Total nitrogen.
November 5, 1909.	*c. c.*	*grams.*
$9^h 00^m$ a.m. to $10^h 00^m$ a.m.	100	0.54
10 00 a.m. 11 00 a.m.	128	.67
11 00 a.m. 12 00 noon	153	.80

METABOLISM EXPERIMENT NO. A 10.

Date, November 5, 1908. Naked body-weight, 48.8 kilograms.

In this and in experiments A 11 to A 15, the subject took food immediately preceding the experiment. He entered the chair calorimeter at 7^h 36^m a. m. and then ate 220 grams of beefsteak, free from fat, and cooked until medium done. A small amount of butter, also pepper and salt, were served with the steak. The experiment began at 8^h 28^m a. m. and continued for three 2-hour periods. No water was taken during the experiment. The subject used the telephone at the end of every period and, according to the observer, he seemed more restless during this experiment than he had been previously, but as no pneumograph curve was obtained we have no method of confirming this. The pulse-rate observations were made by the subject himself, and ranged from 77 to 85, but no body-temperatures were obtained. The subject stated after the experiment that he relished the steak and felt better in this experiment than in the one which was made with him the day before, which was a fasting experiment. The averages for the pulse-rate and the measurements of the metabolism are given in table 29. The statistics for the urine are also given in table 30.

TABLE 29.—*Measurements of metabolism—Metabolism experiment No. A 10.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.[1]
			Carbon dioxide eliminated.	Oxygen absorbed.				
November 5, 1908.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
8^h 28^m a.m. to 10^h 28^m a.m..	42.9	55.1	182	322	28.7	...	142	84
10 28 a.m. 12 28 p.m..	43.9	44.2	186	258	42.5	.73	143	81
12 28 p.m. 2 28 p.m..	41.0	43.9	174	256	35.3	.68	135	81
Total 6 hours[2]......	127.8	143.2	181	278	106.5	...	420	..

[1] Pulse by the subject.
[2] Carbon dioxide per kilogram per minute, 3.71 c. c.; oxygen per kilogram per minute, 5.70 c. c.; heat eliminated per kilogram per hour, 1.43 calories.

TABLE 30.—*Statistics of urine—Metabolism experiment No. A 10.*

Date and period.	Quantity.	Total nitrogen.	Sugar.	
			Polarization.	Titration.
November 5–6, 1908.	*grams.*	*grams.*	*grams.*	*grams.*
7^h 24^m a.m. to 9^h 22^m a.m....................	303	1.46	7.9	8.9
9 22 a.m. 10 28 a.m....................	210	1.11	6.7	7.0
10 28 a.m. 12 28 p.m....................	329	1.99	10.6	9.8
12 28 p.m. 2 28 p.m....................	184	1.37	5.2	5.7
2 28 p.m. 7 00 a.m....................	1140 c. c.	8.60	22.8	42.5

METABOLISM EXPERIMENT No. A 11.

Date, November 19, 1908. Naked body-weight, 52.8 kilograms.

The subject entered the apparatus at 8h 09m a. m., and as in the preceding experiment, was given cooked beefsteak. Of this, he ate 237 grams, finishing at 8h 41m a. m. The experiment began at 8h 50m a. m. and continued for three 2-hour periods. The subject telephoned three times during the experimental period in connection with the collection of the urine. No water was taken during the experiment. The pulse-rate was recorded by the subject himself and ranged from 64 to 74. The body-temperature records were also made by the subject sublingually with a clinical thermometer. The measurements of the metabolism and the average pulse-rates are given in table 31. The statistics for the urine are given in table 32.

TABLE 31.—*Measurements of metabolism—Metabolism experiment No. A 11.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.[1]
November 19, 1908.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
8h 50m a.m. to 10h 50m a.m. .	44.8	43.1	190	251	50.8	0.76	153	72
10 50 a.m. 12 50 p.m. .	45.4	46.3	193	270	53.3	.71	152	68
12 50 p.m. 2 50 p.m. .	42.2	43.8	179	256	45.7	.70	147	65
Total 6 hours[2]......	132.4	133.2	187	259	149.8	....	[3]452	..

[1] Pulse by the subject.
[2] Carbon dioxide per kilogram per minute, 3.54 c. c.; oxygen per kilogram per minute, 4.91 c. c.; heat eliminated per kilogram per hour, 1.42 calories.
[3] Body-temperature at beginning, 98.05° F.; at end, 97.85° F. Heat production for total 6 hours, 447 calories.

TABLE 32.—*Statistics of urine—Metabolism experiment No. A 11.*

Date and period.	Quantity.	Total nitrogen.	Sugar. Polarization.	Sugar. Titration.
November 19–20, 1908.	*grams.*	*grams.*	*grams.*	*grams.*
7h 00m a.m. to 8h 50m a.m.	117	0.85	3.7	3.9
8 50 a.m. 10 50 a.m.	297	1.87	10.1	10.2
10 50 a.m. 12 50 p.m.	194	1.58	6.2	6.7
12 50 p.m. 2 50 p.m.	134	1.39	3.8	4.3
2 50 p.m. 7 00 a.m.	1710 c. c.	11.72	42.8	45.8

METABOLISM EXPERIMENT No. A 12.

Date, November 23, 1908. Naked body-weight, 53.8 kilograms.

The subject entered the chair respiration chamber at 8h 10m a. m. and began eating at 8h 56m a. m., finishing at 9h 11m a. m., during which time he took 75 grams of white bread and 25 grams of dextrose, together with a small cup of hot coffee. The experiment began at 9h 20m a. m., and continued for three 2-hour

periods. The subject used the telephone three times and drank no water during the experiment. He said after the experiment that while he felt all right, he was still very hungry and that he could have eaten 10 times as much food as was given him. The pulse-rate was taken by the subject himself, and ranged from 63 to 75. The body-temperature measurements were taken by the subject sublingually with a clinical thermometer. The average pulse-rates and the metabolism measurements are given in table 33. The statistics for the urine are given in table 34.

TABLE 33.—*Measurements of metabolism—Metabolism experiment No. A 12.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.[1]
			Carbon dioxide eliminated.	Oxygen absorbed.				
November 23, 1908.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
$9^h 20^m$ a.m. to $11^h 20^m$ a.m.	42.4	41.2	180	240	58.8	0.75	152	72
11 20 a.m. 1 20 p.m.	38.3	38.5	162	225	52.9	.72	139	68
1 20 p.m. 3 20 p.m.	37.3	36.9	158	215	48.5	.74	129	64
Total 6 hours [2]	118.0	116.6	167	227	160.2	....	[3]420	..

[1] Pulse rate taken by the subject.
[2] Carbon dioxide per kilogram per minute, 3.10 c. c.; oxygen per kilogram per minute, 4.22 c. c.; heat eliminated per kilogram per hour, 1.30 calories.
[3] Body-temperature at beginning, 97.7° F.; at end, 97.35° F. Heat production for total 6 hours, 412 calories.

TABLE 34.—*Statistics of urine—Metabolism experiment No. A 12.*

Date and period.	Quantity.	Specific gravity.	Total nitrogen.	Sugar.	
				Polarization.	Titration.
November 22–23, 1908.	*grams.*		*grams.*	*grams.*	*grams.*
$7^h 00^m$ a.m. to $1^h 00^m$ p.m.	628	1.036	3.13	38.9	39.4
1 00 p.m. 7 00 p.m.	745	1.029	4.01	23.8	24.5
7 00 p.m. 1 00 a.m.	430	1.026	3.48	5.2	7.1
1 00 a.m. 7 00 a.m.	250	1.024	2.37	3.3	5.6
November 23–24, 1908.					
$7^h 00^m$ a.m. to $9^h 20^m$ a.m.	68	....	.60	3.4	4.0
9 20 a.m. 11 20 a.m.	232	....	1.13	17.6	18.5
11 20 a.m. 1 20 p.m.	190	....	.99	14.6	15.4
1 20 p.m. 3 20 p.m.	100	....	.64	7.2	7.9
3 20 p.m. 7 00 p.m.	350 c. c.	1.027	1.88	....	11.5
7 00 p.m. 1 00 a.m.	665 c. c.	1.023	4.02	8.0	11.0
1 00 a.m. 7 00 a.m.	365 c. c.	1.027	3.10	6.6	9.3

METABOLISM EXPERIMENT NO. A 13.

Date, November 24, 1908. Naked body-weight, 53.6 kilograms.

This experiment was a duplicate of the previous experiment and the subject ate 75 grams of white bread and 25 grams of dextrose after entering the chamber at 8 a. m. He began eating at $8^h 52^m$ a. m. and finished at $9^h 16^m$ a. m. He also drank 200 c. c. of coffee. The experiment began at $9^h 20^m$ a. m. and continued

for three 2-hour periods. No water was taken during the experiment. The subject said that the time did not pass so rapidly as in the previous experiments, that he was hungry, and that the coffee did not taste so good as the coffee given him the day before. The pulse-rate as taken by the subject ranged from 61 to 73. The measurements of the body-temperature were taken sublingually with the clinical thermometer. The results of the metabolism measurements and the average pulse-rates are given in table 35. The statistics for the urine are given in table 36.

TABLE 35.—*Measurements of metabolism—Metabolism experiment No. A 13.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.[1]
			Carbon dioxide eliminated.	Oxygen absorbed.				
November 24, 1908.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
$9^h 20^m$ a.m. to $11^h 20^m$ a.m.	39.8	42.0	169	245	58.8	0.69	144	72
11 20 a.m. 1 20 p.m.	37.9	37.2	161	217	53.9	.74	132	67
1 20 p.m. 3 20 p.m.	37.4	37.2	159	217	49.1	.73	132	63
Total 6 hours[2]	115.1	116.4	163	226	161.8	....	[3]408	..

[1] Pulse by the subject.
[2] Carbon dioxide per kilogram per minute, 3.04 c. c.; oxygen per kilogram per minute, 4.22 c. c.; heat eliminated per kilogram per hour, 1.27 calories.
[3] Body-temperature, at beginning, 97.7° F.; at end, 97.5° F. Heat production for total 6 hours, 403 calories.

TABLE 36.—*Statistics of urine—Metabolism experiment No. A 13.*

Date and period.	Quantity.	Total nitrogen.	Sugar.	
			Polarization.	Titration.
November 24–25, 1908.	*grams.*	*grams.*	*grams.*	*grams.*
$7^h 00^m$ a.m. to $9^h 20^m$ a.m.	176	1.23	5.3	7.5
9 20 a.m. 11 20 a.m.	238	1.11	16.6	17.7
11 20 a.m. 1 20 p.m.	214	1.05	15.9	16.3
1 20 p.m. 3 20 p.m.	109	.67	7.3	7.9
3 20 p.m. 7 00 p.m.	340 c. c.	1.93	....	15.2
7 00 p.m. 1 00 a.m.	718 c. c.	4.24	....	9.0
1 00 a.m. 7 00 a.m.	370 c. c.	2.92	....	8.1

METABOLISM EXPERIMENT No. A 14.

Date, April 5, 1909. Naked body-weight, 52.3 kilograms.

The subject entered the respiration chamber at $7^h 57^m$ a. m., and between $8^h 04^m$ a. m. and $8^h 24^m$ a. m. ate 258 grams of cooked beefsteak. The experiment began at $8^h 36^m$ a. m., continuing for four 1-hour periods. No water was taken by the subject. A small Tungsten lamp, producing 3.7 calories per hour, was used for the first time in this experiment to illuminate the interior of the chamber, and the subject stated that the light from it was very good, and that he found it much easier to read when this lamp was in use. The pulse- and respiration-

rates were obtained by means of the stethoscope and pneumograph, the range for the pulse-rate being from 83 to 100, and for the respiration-rate from 16 to 21. The body-temperature measurements were made with the electrical-resistance thermometer in the rectum. The measurements of the metabolism and the average pulse- and respiration-rates are given in table 37. The statistics for the urine are given in table 38.

TABLE 37.—*Measurements of metabolism—Metabolism experiment No. A 14.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
April 5, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
8^h36^m a.m. to 9^h36^m a.m.	22.4	19.9	190	232	25.6	0.82	80	92	17
9 36 a.m. 10 36 a.m.	23.8	21.4	202	250	27.7	.81	82	92	17
10 36 a.m. 11 36 a.m.	24.4	24.4	207	285	28.0	.73	81	90	18
11 36 a.m. 12 36 p.m.	24.5	22.3	208	260	27.9	.80	81	89	19
Total 4 hours [1].....	95.1	88.0	202	257	109.2	....	[2]324	..	..

[1] Carbon dioxide per kilogram per minute, 3.86 c. c.; oxygen per kilogram per minute, 4.91 c. c.; heat eliminated per kilogram per hour, 1.55 calories.
[2] Rectal body-temperature at beginning, 36.82° C.; at end, 37.56° C. Heat production for total 4 hours, 356 calories.

TABLE 38.—*Statistics of urine—Metabolism experiment No. A 14.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
April 1–2, 1909	*c. c.*		*grams.*	*grams.*
7^h00^m a.m. to 7^h00^m p.m..................	1301	....	4.58	60.5
7 00 p.m. 7 00 a.m..................	1504	....	6.74	50.4
April 4–5, 1909				
12^h00^m p.m. to 7^h00^m a.m..................	408	....	2.70	14.4
April 5, 1909.				
7^h00^m a.m. to 8^h36^m a.m..................	77	1.031	.52	3.4
8 36 a.m. 10 36 a.m..................	266	1.030	1.63	11.5
10 36 a.m. 12 36 p.m..................	250	1.029	1.77	10.4

METABOLISM EXPERIMENT No. A 15.

Date, May 5, 1909. Naked body-weight, 49.5 kilograms.

Previous to entering the calorimeter chamber for this experiment, the subject ate 261 grams of cooked beefsteak. Two hours afterwards, at $10^h 54^m$ a. m., he entered the calorimeter chamber. The experiment began at $11^h 46^m$ a. m. and continued for four 1-hour periods. There was no water consumed during the experiment. By means of the stethoscope and pneumograph, the pulse- and respiration-rates were obtained, the former ranging from 86 to 107, and the latter from 14 to 18. The rectal body-temperatures were taken with the electrical-resistance thermometer. The measurements of the metabolism and the average pulse- and respiration-rates are given in table 39. The statistics for the urine are given in table 40.

TABLE 39.—*Measurements of metabolism—Metabolism experiment No. A 15.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
May 5, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
11h 46m a.m. to 12h 46m p.m.	25.7	26.6	218	310	28.8	0.70	85	100	15
12 46 p.m. 1 46 p.m.	23.5	21.2	199	247	27.9	.81	76	92	15
1 46 p.m. 2 46 p.m.	23.5	24.7	199	288	28.3	.69	76	94	16
2 46 p.m. 3 46 p.m.	21.2	19.5	180	228	26.5	.79	78	93	16
Total 4 hours [1].....	93.9	92.0	199	268	111.5	....	[2]315	..	..

[1] Carbon dioxide per kilogram per minute, 4.02 c. c.; oxygen per kilogram per minute, 5.41 c. c.; heat eliminated per kilogram per hour, 1.60 calories.
[2] Rectal body-temperature at beginning, 37.25° C.; at end, 37.33° C. Heat production for total 4 hours, 319 calories.

TABLE 40.—*Statistics of urine—Metabolism experiment No. A 15.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
May 4–5, 1909.	*c. c.*		*grams.*	*grams.*
7h 00m a.m. to 7h 00m p.m.	1520	1.026	6.21	54.0
7 00 p.m. 7 00 a.m.	1552	1.024	7.05	60.7
May 5, 1909.				
7h 00m a.m. to 11h 48m a.m.	97	1.025	.53	4.0
11 48 a.m. 1 48 p.m.	236	1.026	1.51	9.0
1 48 p.m. 3 48 p.m.	200	1.026	1.44	6.8

METABOLISM EXPERIMENT No. A 16.

Date, March 11, 1910. Naked body-weight, 49.8 kilograms.

The subject took a cup of clear coffee at 7 a. m. and then came to the laboratory without breakfast, and at 8h 15m a. m. entered the chair calorimeter. The experiment began at 8h 59m a. m. and continued for three 1-hour periods. No water was taken. The subject stated that he was not uncomfortable in any way.

TABLE 41.—*Measurements of metabolism—Metabolism experiment No. A 16.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
March 11, 1910.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
8h 59m a.m. to 9h 59m a.m.	20.2	20.1	171	235	20.6	0.73	60	73	14
9 59 a.m. 10 59 a.m.	18.5	18.1	157	211	20.6	.74	58	72	13
10 59 a.m. 11 59 a.m.	19.1	18.5	162	216	21.2	.75	58	69	13
Total 3 hours [1].....	57.8	56.7	164	221	62.4	....	[2]176	..	..

[1] Carbon dioxide per kilogram per minute, 3.29 c. c.; oxygen per kilogram per minute, 4.44 c. c.; heat eliminated per kilogram per hour, 1.18 calories.
[2] Rectal body-temperature at beginning, 36.55° C.; at end, 36.91° C. Heat production for total 3 hours, 193 calories.

The pulse- and respiration-rates were recorded by means of the stethoscope and pneumograph, the pulse-rates ranging from 66 to 84 and the respiration-rate from 12 to 16. The body-temperature measurements were obtained by means of the electrical-resistance thermometer. The subject was very quiet throughout the experiment and was asleep a short time, at about $10^h\ 30^m$ a. m. He used the telephone at the end of each period.

The hourly averages of the pulse- and respiration-rates and the measurements of the metabolism are given in table 41 herewith. The statistics for the urine are given in table 42.

TABLE 42.—*Statistics of urine—Metabolism experiment No. A 16.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
March 11, 1910.	*c. c.*		*grams.*	*grams.*	
7^h00^m a.m. to 9^h10^m a.m.......	227	1.027	0.78	7.6	9.74
9 10 a.m. 10 10 a.m.......	107	1.027	.38	3.7	9.74
10 10 a.m. 11 13 a.m.......	96	1.027	.35	3.3	9.43
11 13 a.m. 12 08 p.m.......	128	1.028	.51	4.4	8.63

COMPARISON OF EXPERIMENTS WITH CASE A.

With this subject, nine experiments were made under conditions that are practically comparable, namely, 12 hours after the last meal, sitting quietly inside of the chair calorimeter. During the first two periods of another experiment, previous to the ingestion of food, the subject was also under the same conditions. These experiments have been collected, together with several experiments which followed the ingestion of food, and a summary of the results is given in table 43.

The investigations with this subject continued for more than a year and consequently we have an opportunity for comparing the metabolism at different times and noting the degree of regularity. From a comparison with the general clinical picture presented by this subject at different periods of the study of his disease, we find that when he was in the lowest condition and the acidosis was at its highest, namely, in the spring of 1909, the katabolism as measured by the carbon-dioxide excretion, oxygen absorption, and heat-elimination was, as a rule, somewhat higher than in other periods with this subject.

In considering the results given in the table it is important to bear in mind that the experiment of March 4, when an unusually low katabolism is indicated, was made in the bed calorimeter, under a condition of body-rest which is shown in a subsequent discussion to result in a depressed metabolism amounting to some 20 per cent below the value obtained when the subject is sitting upright. The carbon-dioxide excretion in the experiments without food varied from 161 c. c. to 186 c. c. per minute, and the oxygen consumption from 218 c. c. in the experiment with the bed calorimeter, and 221 c. c. in the experiment of March 11, 1910, in the chair calorimeter, to 256 c. c. In the experiments following

the ingestion of food, on the other hand, we find a marked increase in the oxygen absorption when beefsteak was given, and hardly any increase following the ingestion of carbohydrate. The discussion regarding the influence of the ingestion of food on the metabolism of diabetics is, however, taken up in detail in a subsequent chapter.

The average pulse-rate undergoes a marked variation, the range being from 65 to 91 per minute. During the experiment in the bed calorimeter the pulse-rate was abnormally high for this subject, and when compared with the other

TABLE 43.—*Comparison of metabolism experiments with Case A.*

EXPERIMENTS WITHOUT FOOD.

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Respiratory quotient.	Heat eliminated per hour.	Heat produced per hour.	Average pulse per minute.	Average respiration per minute.
		kilos.	*hrs.*	*c. c.*	*c. c.*		*cals.*	*cals.*		
A 1	Nov. 4, 1908	48.8	6	165	237	0.70	70	[11] 70	81	....
A 2	Nov. 18, 1908	52.8	6	161	229	.70	67	65	67	....
A 3	Dec. 16, 1908	57.3	6	186	251	.74	76	77	65	....
A 4	Mar. 4, 1909 [1]	51.6	3	166	218	.76	59	64	82	15.5
A 5*a*	Mar. 13, 1909	51.4	2	173	253	.68	77	76	90	18.5
A 6	Mar. 19, 1909 [2]	51.4	4	181	250	.72	73	..	86	18.0
A 7	Mar. 26, 1909 [3]	52.2	4	167	235	.71	70	73	84	17.0
A 8	May 17, 1909	49.5	4	170	256	.66	70	71	82	17.0
A 9	Nov. 5, 1909	53.8	3	163	222	.73	64	67	70	15.0
A 16	Mar. 11, 1910	49.8	3	164	221	.74	59	64	71	13.5
EXPERIMENTS WITH FOOD.										
A 10	Nov. 5, 1908 [4]	48.8	6	181	278	0.65	70	[11] 70	82	....
A 11	Nov. 19, 1908 [5]	52.8	6	187	259	.72	75	75	68	....
A 12	Nov. 23, 1908 [6]	53.8	6	167	227	.74	70	69	68	....
A 13	Nov. 24, 1908 [7]	53.6	6	163	226	.72	68	67	67	....
A 5*b*	Mar. 13, 1909 [8]	51.4	2	183	243	.75	73	85	86	18.0
A 14	Apr. 5, 1909 [9]	52.3	4	202	257	.79	81	89	91	18.0
A 15	May 5, 1909 [10]	49.5	4	199	268	.74	79	80	95	15.5

[1] Bed calorimeter.
[2] 40 minutes before the experiment began, the subject finished drinking one cup of hot coffee (without sugar or milk). At the beginning of the third period he drank a cup of cold coffee.
[3] 45 minutes before the experiment began, the subject finished drinking one cup of hot, clear, strong coffee. At the beginning of the third hour he drank one cup (137 grams) of cold clear coffee.
[4] About 20 minutes before the experiment began, the subject finished eating 220 grams of cooked beefsteak.
[5] 9 minutes before the experiment began, the subject finished eating 237 grams of cooked beefsteak.
[6] 9 minutes before the experiment began, the subject finished eating 75 grams of white bread and 25 grams of dextrose together with a small cup of hot coffee.
[7] 4 minutes before the experiment began, the subject finished eating 75 grams of bread and 25 grams of dextrose together with 200 c. c. of coffee infusion.
[8] At the beginning of the third hour, the subject ate 25 grams of dextrose and 75 grams of white bread and a cup of cold coffee.
[9] 12 minutes before the experiment began, the subject finished eating 258 grams of cooked beefsteak.
[10] 3 hours and 11 minutes before the experiment began, the subject finished eating 261 grams of cooked beefsteak.
[11] Heat eliminated and not heat produced.

observations made in the laboratory in experiments without food, is unusually high. In the first experiment made with this subject he took his own pulse-rate, and the records show that it was somewhat above his normal rate, due unquestionably to the psychical effect of an initial experiment.

An examination of the respiratory quotients shows that aside from the experiment of March 4 made in the bed calorimeter, the quotients as a rule were 0.7, or below, while in the last two experiments, when the subject was in unusually good condition, it was somewhat higher, indicating the oxidation of a somewhat larger proportion of carbohydrates.

The variations in the metabolism measurements may or may not indicate actual variations in the metabolism of the subject. Theoretically, the subject should have remained absolutely quiet, with the greatest enforced muscular rest, and under the conditions stipulated by Zuntz and Johansson in their researches upon the respiratory exchange. Practically, it is not feasible to retain diabetics for this period with enforced muscular relaxation, as they are weak and not in a normal condition. On the other hand, this particular subject was especially quiet in the calorimeter, with only slight muscular movements; he did not leave the chair, and sat for the most part quietly reading. While the individual experiments may not have the absolutely accurate value that they would be expected to have when made under the conditions imposed by Johansson, nevertheless, the average of all the experiments should indicate the metabolism of this subject when sitting quietly at rest, and the variations are no larger than one would expect with the conditions under which the experiments were made.

Judging from the comparison table, therefore, it will be seen that this subject in the course of 1 year underwent no material alteration in the general metabolism when food was not taken. It is difficult to point out any striking relationship existing between the respiratory exchange and the general condition of the subject, and yet the tendency for a higher metabolism during the severe acidosis is wholly in line with the general view that the more severe the diabetes the greater the metabolism.

GROUP I. CASE B.

DESCRIPTION OF THE CASE.

Female; born September 9, 1869; married; doing her own housework; first recognized symptoms of diabetes mellitus at the age of 39, December 25, 1908; came under observation, September, 1909.

Family history.—No history of diabetes in the family. Father died of typhoid fever, mother of apoplexy, and one sister at child-birth. One brother and four sisters are well.

Past history.—Measles, mumps, whooping cough, scarlet fever. Pneumonia, December 25, 1908. One miscarriage.

Present illness.—Diabetes mellitus was first recognized because of pruritus vaginæ December 25, 1908. At that time the quantity of urine in 12 hours was

approximately 2000 c. c. Polyphagia, polydipsia, weakness, cramps in the legs, slight dizziness, and poor eyesight were the other prominent symptoms. Constipation, moderate dyspnea, and palpitation were also present in September, 1909.

Physical examination.—An emaciated, weary woman. Greatest weight, 50.6 kilograms; weight, September 1, 1909, 38.9 kilograms; usual weight, 46.1 kilograms. Height, 158 centimeters. Marked odor to breath usually attributed to acetone, but upon this doubt has been thrown by Folin. Blood-pressure, 110 m. m. (Riva Rocci); pulse, 84. No enlarged axillary, cervical or inguinal glands. Heart: 3 centimeters to right of median line and 2 centimeters external to left mammillary line. Systolic murmur at the apex transmitted to the axilla. Lungs: scattered râles throughout the chest, not permanently present. Abdomen: liver, kidneys, and spleen palpable, but not enlarged. Knee jerks present; no edema.

Urine data.—The quantity of urine was usually 2000 to 2500 c. c. It increased to 3060 c. c. the first day upon which 24 grams of sodium bicarbonate were administered. Coincidently, the diet was being restricted in carbohydrates. At this time the weight rose from 39.2 kilograms upon September 24 to 40.8 kilograms upon September 28. The edema was manifest, as in Case A, under similar conditions.

The reaction of the urine remained acid throughout the period of observation, although at one period 24 grams of sodium bicarbonate were given daily for over 2 weeks, with the exception of 1 day when 16 grams were given. The large quantity of diacetic acid was another evidence of the extent of the acidosis. Three determinations of ammonia showed approximately 3 grams. Still another proof was shown by the levo-rotation of 0.5 per cent in terms of glucose after fermentation upon January 17, 1910.

The history of the case is shown by the chart herewith, table 44.

EXPERIMENTS WITH CASE B.

With this subject, one metabolism experiment was made and four respiration experiments. The bed calorimeter was used for the metabolism experiment. The vital statistics were as follows:

Date of birth, September 9, 1869; height, 158 centimeters; range in naked body-weight, 40.5 kilograms to 42.2 kilograms.

METABOLISM EXPERIMENT No. B 1.

Date, March 2, 1910. Naked body-weight, 41.2 kilograms.

The subject came to the laboratory in the morning without breakfast, after a 12-hours' fast, and entered the chamber of the bed calorimeter at $8^h\ 36^m$ a. m. The measurements of the pulse- and respiration-rates, and of the muscular activity were made with the stethoscope and pneumograph, which were adjusted before the subject entered the apparatus. Clinical thermometers were used for measuring the body-temperature in this experiment. The experiment began at $9^h\ 26^m$ a. m. and continued for three 1-hour periods, ending at $12^h\ 26^m$ p. m. The pulse-

TABLE 44.—*Clinical chart—Case B.*

Date.	Expt. No.	Volume of urine.	Specific gravity.	Diacetic acid.	Nitrogen.	Ammonia.		Sugar.		Diet.		Carbohydrate balance.	NaHCO₃.	Naked body-weight.	Remarks.
						Total.	$\frac{NH_3 - N}{\text{Total N.}}$	By Citron.	By rotation.	Carbohydrate.	Alcohol.				
1909.		*c. c.*			*gms.*	*gms.*	*p. ct.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*	
Sept. 1		....	1034	+	..	..	..	..	[1] 6.2	..	..	....	..	38.9	
Sept. 7–8		....	1034	+ +	..	..	..	..	[1] 6	150	6	....	0	38.3	
Sept. 8–9		2400	1034	+ +	..	..	..	..	125	110	6	—15	0	38.2	
Sept. 9–10		2325	1034	+ + +	..	..	..	..	107	105	6	0	6	37.5	
Sept. 10–11		2355	1031	+ + +	..	..	..	..	94	100	6	+ 5	6	38.1	
Sept. 11–12		2535	1029	+ +	..	..	..	..	86	85	6	0	6	38.6	
Sept. 12–13		2550	1031	+ + +	..	..	..	..	92	75	6	—15	6	38.6	
Sept. 13–14		1800	1031	+ +	..	..	..	..	68	70	6	0	6	38.9	
Sept. 14–15		2250	1029	+ + +	..	..	..	..	77	70	6	— 5	6	39.4	
Sept. 15–16		2445	1023	+ +	10.6	..	..	..	56	60	6	+ 5	6	39.1	
Sept. 16–17		2460	1023	+ + +	..	..	..	..	49	60	12	+10	6	39.0	
Sept. 17–18		2235	1021	+ +	..	..	..	..	27	20	12	— 5	6	39.0	Vegetables, 375 c. c. cream, yolks 3 eggs, 120 c. c. wine.
Sept. 18–19		1995	1023	+ +	..	..	..	..	40	45	12	+ 5	6	39.4	
Sept. 19–20		2475	1022	+ + +	..	..	..	..	45	45	12	0	6	39.5	
Sept. 20–21		2010	1018	+ +	..	..	..	..	20	20	12	0	6	39.4	As on Sept. 17–18.
Sept. 21–22		2205	1026	+ + + +	..	..	..	..	35	35	12	0	6	39.4	
Sept. 22–23		2460	1021	....	..	..	..	..	30	35	12	+ 5	6	39.5	
Sept. 23–24		3060	1020	+ + + +	..	..	..	..	43	35	12	— 5	24	39.2	
Sept. 24–25		1860	1024	+ + +	..	..	..	..	19	20	12	0	24	39.9	As on Sept. 17–18.
Sept. 25–26		2640	1021	+ + +	..	..	..	..	26	20	12	— 5	24	40.6	Do.
Sept. 26–27		2040	1022	+ + + +	..	..	..	..	16	20	12	+ 5	24	40.6	
Sept. 27–28		2790	1020	+ + + +	..	..	..	..	45	20	12	—25	24	40.9	
Sept. 28–29		1680	....	+ + + +	..	..	..	..	10	20	12	+10	24	40.5	
Sept. 29–30	**B 2**	**2325**	**1021**	+ + + +	..	..	..	..	**19**	**20**	**12**	**0**	**24**	**40.9**	
Sept. 30–Oct. 1		2160	1026	+ + + +	..	..	..	..	26	20	12	— 6	24	42.0	
Oct. 1–2		2055	1020	+ + +	..	..	..	0	0	10	18	+10	24	41.6	Vegetable day.
Oct. 2–3	**B 3**	**1950**	**1021**	+ + + +	..	..	..	**0**	**—4**	**20**	**12**	**+20**	**16**	**41.8**	As on Sept. 17–18.
Oct. 3–4		1920	1024	+ + + +	..	..	..	21	..	15	12	— 5	24	42.1	
Oct. 4–5		1320	1020	+ + + +	..	..	..	9	..	15	12	(?)	24	42.0	
Oct. 5–6		1875	1019	+ + + +	7	..	..	8	..	15	12	+ 5	24	42.2	
Oct. 6–7	**B 4**	**1965**	**1021**	+ + +	..	..	..	**8**	..	**20**	**12**	**+10**	**24**	**42.2**	As on Sept. 17–18.
Oct. 7–8		2190	1024	+ +	..	..	..	39	..	15	12	—25	24	42.4	
Oct. 8–9		1470	1022	+ + + +	..	..	..	..	3	15	12	+10	24	43.0	
Oct. 21–22		1750	1030	....	..	..	..	..	21	15	12	— 5	24	[3]42.2	
Nov. 29–30		1500+	1024	+ + +	..	..	..	..	12	30	12	(?)	12±	41.5	
1910.															
Jan. 2–3		2000	1023	+ +	..	..	..	..	32	30	12	0	4	40.8	
Jan. 16–17		2125	1026	+ + + +	..	2.8	..	+	43	40	12	— 5	0	41.4	
Feb. 10–11		1750	1024	+ + +	..	..	..	..	4	15	12	+10	20	....	Vegetable day.
Feb. 13–14		1750	1027	+ + +	5.33	..	..	69	56	65	12	+10	20	41.5	
Feb. 28–Mar. 1		2500	1031	+ +	6.98	2.8	33	89	80	..	..	....	..	....	
Mar. 1–2[2]		2363	1023	+ +	8.16	3.1	31.3	46	28	..	..	....	..	42.0	

[1] Per cent. [2] β-oxybutyric acid on this date was 11.0 grams. [3] Oct. 26, 1909.

rate ranged from 56 to 67 and the respiration-rate from 14 to 18. The subject slept the greater part of the first period, but in the second period was awake most of the time. In the last period, she slept about 15 minutes at the beginning of the period.

The measurements of the metabolism and the average pulse- and respiration-rates are given in table 45, and the statistics of urine in table 46. The experiment seemed to be satisfactory as a whole.

TABLE 45.—*Measurements of metabolism—Metabolism experiment No. B 1.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
March 2, 1910	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
9h 26m a.m. to 10h 26m a.m.	15.5	....	132	....	23.6	....	47	62	15.0
10 26 a.m. 11 26 a.m.	15.8	15.6	134	182	23.2	0.74	53	60	16.0
11 26 a.m. 12 26 p.m.	15.9	15.6	135	182	22.7	.74	53	58	16.5
Total 3 hours [1].....	47.2	[2]31.2	133	[2]182	69.5	[2]0.74	[3]153	60	16.0

[1] Carbon dioxide eliminated per kilogram per minute, 3.23 c. c.; oxygen absorbed per kilogram per minute, 4.42 c. c.; heat eliminated per kilogram per hour, 1.24 calories.
[2] Does not include period 9h 26m a. m. to 10h 26m a. m.
[3] Sublingual body-temperature at beginning, 36.45° C.; at end, 36.45° C. Heat production for total 3 hours, 153 calories.

TABLE 46.—*Statistics of urine—Metabolism experiment No. B 1.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
March 1–2, 1910.	*c. c.*		*grams.*	*grams.*	
2h 00m p.m. to 5h 00m p.m.	230	1.026	0.46	8.0	....
5 00 p.m. 6 45 p.m.	199	1.028	0.56	7.8	....
6 45 p.m. 8 45 p.m.	330	1.029	1.18	10.9	....
8 45 p.m. 11 45 p.m.	275	1.027	1.19	7.6	....
11 45 p.m. 2 15 a.m.	136	1.028	0.68	2.6	....
2 15 a.m. 5 00 a.m.	116	1.027	0.60	1.9	....
5 00 a.m. 7 30 a.m.	83	....	0.49	1.5	....
March 2–3, 1910.					
7h 30m a.m. to 12h 30m p.m.	470	1.019	1.60	4.3	2.69
12 30 p.m. 2 30 p.m.	114	....	0.42	0.3	.71
2 30 p.m. 6 45 p.m.	410	1.012	1.03	0.3	.29
6 45 p.m. 8 00 p.m.	32	....	0.14	0.1	....
8 00 p.m. 9 30 p.m.	34	....	0.15	0.2	....
9 30 p.m. 1 30 a.m.	197	1.023	0.77	1.8	....
1 30 a.m. 5 30 a.m.	310	1.027	0.94	8.5	....
5 30 a.m. 7 00 a.m.	78	1.029	0.27	1.9	....

RESPIRATION EXPERIMENT No. B 2.

Date, September 29, 1909. Naked body-weight, 40.5 kilograms.

This experiment included four separate periods, the first 10 minutes long, and the last three 13 or 14 minutes in length. On the morning of the experiment, the subject came from a nearby hospital where she had been kept on a diabetic

regimen and lay down on the couch for some 20 minutes before the first period began. In this period the closure of the nosepieces was not wholly satisfactory, but the results appeared to be reasonably accurate. In the last experiment the subject became very restless and opened her mouth just as the valve was thrown. The patient was rather weak and complained of some tenderness about the nose, but other than that, she cooperated in the experiment very fully and, as a whole, the results were good. The results of the experiment are given in table 47.

TABLE 47.—*Results of respiration experiment No. B 2.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
September 29, 1909.	*m.* *s.*	*c. c.*	*c. c.*			
8h 20m a.m.	10 3	127	169	0.75	71	15
8 40 a.m.	13 59	118	177	.67	70	15
9 06 a.m.	14 2	117	175	.67	69	14
9 30 a.m.	12 46	128	172	.75	67	14
Average[1]	.. ..	123	173	0.71	69	15

[1] Carbon dioxide eliminated per kilogram per minute, 3.04 c. c.; oxygen absorbed per kilogram per minute, 4.27 c. c.

RESPIRATION EXPERIMENT No. B 3.

Date, October 2, 1909. Naked body-weight, 41.6 kilograms.

The subject spent the time intervening between this experiment and the one preceding in the hospital and fasted the day before the experiment. She came to the laboratory without breakfast and lay on the couch for at least 5 minutes before the experiment began. Four separate periods were included in this day's experiment, varying from 10 to 15 minutes in length. Unfortunately, the oxygen determinations were lost in the second and fourth periods, and consequently the respiratory quotients can not be computed. Owing to the fasting of the preceding day, the subject appeared to be very weak. The nosepieces had been more carefully adjusted in this experiment and they gave the subject no discomfort. The results of the experiment are given in table 48.

TABLE 48.—*Results of respiration experiment No. B 3.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
October 2, 1909.	*m.* *s.*	*c. c.*	*c. c.*			
8h 24m a.m.	10 3	132	171	0.77	62	17
8 42 a.m.	15 ..	119	...	....	66	16
9 06 a.m.	10 2	122	167	0.73	69	15
9 23 a.m.	14 57	125	...	....	67	17
Average[1]	.. ..	125	169	0.75	66	16

[1] Carbon dioxide eliminated per kilogram per minute, 2.99 c. c.; oxygen absorbed per kilogram per minute, 4.04 c. c.

RESPIRATION EXPERIMENT NO. B 4.

Date, October 6, 1909. Naked body-weight, 42.2 kilograms.

The subject came to the laboratory at 8 o'clock from the hospital, without breakfast, and lay down on the couch for nearly half an hour before the experiment began. Adhesive plaster was placed over the lips and the nosepieces were inserted very firmly. There were four separate periods, lasting from 10 to 15 minutes each. After the first period the subject said that she did not wish the nosepieces released or the plaster covering the mouth removed, so they were not changed in any way. In the last two periods the subject became more restless, and after the experiment was over she complained that her back ached. At 10 a. m., after the conclusion of the last period, 128 c. c. of urine were passed. The results of the experiment are given in table 49.

TABLE 49.—*Results of respiration experiment No. B 4.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
October 6, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
8h 28m a.m.	10	6	126	187	0.67	64	15
8 44 a.m.	14	47	119	188	.63	68	14
9 09 a.m.	14	46	124	165	.75	67	15
9 34 a.m.	13	20	136	187	.73	65	15
Average[1]	..	..	126	182	0.70	66	15

[1] Carbon dioxide eliminated per kilogram per minute, 2.99 c. c.; oxygen absorbed per kilogram per minute, 4.31 c. c.

RESPIRATION EXPERIMENT NO. B 5.

Date, March 2, 1910. Naked body-weight, 41.2 kilograms.

After the calorimeter experiment of this date the subject lay on a couch for about 4 hours, taking no food. The experiment here described, therefore, followed a fast of some 20 or more hours.

TABLE 50.—*Results of respiration experiment No. B 5.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
March 2, 1910.	*m.*	*s.*	*c. c.*	*c. c.*			
4h 35m p.m.	10	3	135	....	....	61	13
4 58 p.m.	15	6	123	....	....	61	14
5 23 p.m.	14	58	122	....	....	60	11
5 52 p.m.	15	0	133	179	0.74	60	12
6 24 p.m.	10	3	131	184	0.71	60	13
Average[1]	..	..	129	182	0.73	60	13

[1] Carbon dioxide eliminated per kilogram per minute, 3.23 c. c.; oxygen absorbed per kilogram per minute, 4.42 c. c.

This respiration experiment was divided into five separate periods, the first of 10 minutes, and the remaining periods about 15 minutes in length. During the second period the subject was very restless, and in the third period there seemed to be a leak about the mouth, owing to imperfect closure with the surgeon's plaster. A new supply of adhesive plaster was used for the fourth period and the liability to leakage was thus diminished. In the intermission between the periods, the nosepieces were removed and reinflated. The results of the experiment are given in table 50.

GROUP I. CASE C.

DESCRIPTION OF THE CASE.

Male; born September 24, 1879; married; dentist; developed diabetes at the age of 28, September, 1908; came under observation March 23, 1909.

Family history.—No family history of diabetes. Father died of malignant disease of the lung; mother and one sister are well. No children.

Past history.—Measles, mumps, whooping cough. Malaria at 14. The patient did extra work for financial reasons while obtaining his education.

Present illness.—The disease began in September, 1908, when polyuria was observed. The onset was fairly acute, coming on during a period of 2 weeks. The greatest volume of urine observed by the patient was 5000 c. c. Polyphagia, polydipsia, polyuria, muscular weakness, balanitis were the chief symptoms, besides the loss of weight. The greatest naked body-weight was 73.5 kilograms, and in September, 1908, it was 71.7 kilograms, falling to 61.7 kilograms in November, 1908. On March 23, 1909, it was 64 kilograms.

Physical examination.—Height, 166 centimeters. Pupils equal and react to light. Tongue and teeth normal. No enlarged cervical, axillary, or inguinal glands. Pulse, 104; blood-pressure (Riva Rocci), 125 mm. Heart and lungs normal. Right kidney movable and palpable throughout. Liver and spleen not recorded abnormal. Slight phimosis. Balanitis.

General treatment and history of case.—The diet was gradually restricted from an indefinite amount of carbohydrate upon March 23, 1909, to about 100 grams carbohydrate April 3, 1909. At the same time the quantity of fat in the diet was increased, and the quantity of albumen decreased. Coincidently the patient observed a gradual increase in strength, which lasted into June. During July he was able to take a sailing trip of 2 weeks upon a small yacht, living meantime upon quite a restricted diet, which at this time was supposed to contain about 50 grams carbohydrates. Following this vacation, the weight decreased and with it his strength, yet the patient was able to carry on his profession, and, in addition, to work in a garden or play tennis.[1] On October 24 he entered the New England Deaconess Hospital, only remaining there until October 31. It was hoped that by accurate tests with the diet and calorimeter it would be found that he could tolerate some form of carbohydrates and the downward course of the disease could be arrested. The hopelessness of the case,

[1] More exercise than was advisable.

TABLE 51.—*Clinical chart—Case C.*

Date.	Experiment No.	Volume of urine.	Specific gravity.	Reaction.	Diacetic acid.	β-oxybutyric acid.	Nitrogen.	Ammonia.		Sugar.	
								Total.	$\frac{NH_3 - N}{Total\ N}$	By Citron.	By rotation.
1909.		*c. c.*				*gms.*	*gms.*	*gms.*	*p. ct.*	*gms.*	*gms.*
Mar. 22–23....	....	4500	1039	ac.	0	....	34.9	...	....	302	306
Mar. 30–31....	....	3000	1035	ac.	+ + +	....	....	...	....	121	90
Apr. 2– 3....	....	4000	1033	ac.	....	....	24.8	3.0	10.0	180	152
Apr. 6– 7....	....	3500	1033	ac.	+ +	....	....	...	....	149	140
Apr. 8– 9....	....	3500	1034	alk.	+ + + +	....	....	...	....	115	...
May 5– 6....	....	2750	1037	ac.	+ +	....	20.8	2.5	9.9	107	110
May 9–10....	....	1500	1034	ac.	+ +	....	15.7	...	....	53	39
May 13–14....	....	2430	....	....	0	5.7	17.9	2.0	9.2	115	...
May 19–20....	....	1875	1031	ac.	+	....	....	...	....	48	45
May 26–27....	....	1870	....	....	....	....	18.9	...	....	89	...
June 3– 4....	....	1750	1035	ac.	+	14.2	....	...	....	...	70
June 6– 7....	....	2250	1035	ac.	+	....	....	3.6	....	96	81
June 7– 8....	....	1735	....	....	....	....	13.2	...	....	104	...
June 10-11.	**C 10**	**2305**	....	....	....	**14.6**	**20.6**	**2.9**	**11.6**	**141**	...
June 13–14....	....	[1]5000	....	....	....	[1]13.0	....	...	....	...	...
June 14-15.	**C 13**	....	....	....	....	**[1]13.0**	**21.8**	...	....	**122**	...
June 17-18.	**C 14**	**1680**	....	....	....	....	**17.2**	...	....	**123**	...
June 21-22.	**C 15**	**2045**	....	....	....	....	**14.3**	...	....	**142**	...
June 23–24....	....	2105	....	....	....	....	22.2	...	....	123	...
June 24-25.	**C 16**	....	....	....	....	....	**22.3**	**2.6**	**9.6**	**123**	...
July 20–21....	....	2500	1034	ac.	+ +	....	16.9	4.1	20.0	...	115
July 26–27....	....	2000	1041	ac.	+ +	....	16.2	...	...	...	124
Aug. 2– 3....	....	2125	1023	ac.	+ +	15.3	17.2	...	....	...	85
Aug. 4– 5....	....	2000	1039	ac.	+ + +	[1]18.5	....	...	....	106	88
Aug. 5– 6....	....	1750	1034	ac.	+ +	[1]18.5	....	...	....	95	74
Aug. 6– 7....	....	2500	....	....	....	....	11.2	...	....	110	...
Aug. 7– 8....	....	2500	....	....	....	14.2	9.0	...	....	...	101
Aug. 8– 9....	....	2625	....	....	....	14.2	13.1	...	....	...	134
Aug. 9-10...	**C 17**	**2375**	**1050**	ac.	+	**14.2**	....	...	....	...	**124**
Aug. 16–17....	....	2750	1043	ac.	+	....	....	...	....	...	182
Aug. 22–23....	....	2750	1039	ac.	+ + +	....	24.4	...	....	160	154
Aug. 23-24.	**C 18**	**2750**	....	....	+ + +	**49.5**	**27.5**	...	....	**170**	**137**
Sept. 4– 5....	....	3000	1038	ac.	0	....	....	...	....	...	198
Sept. 9–10....	....	3000	1040	ac.	0	....	....	...	....	...	222
Sept. 19–20....	....	2750	1038	ac.	Sl. +	....	20.3	...	....	...	149
Sept. 27–28....	....	3250	1032	ac.	+ + +	24.2	17.5	5.0	23.5	114	117
Oct. 7– 8....	....	2900	1030	ac.	+ + +	....	....	...	....	116	...
Oct. 20–21....	....	3750	1032	....	....	33	29.6	...	....	57	...
Oct. 21–22....	....	....	....	....	....	....	16.9	...	....	140	...
Oct. 22–23....	....	3500	1031	....	....	33	22.4	...	....	127	...
Oct. 23–24....	....	3750	1027	....	....	33	20.7	...	....	126	...
Oct. 24–25....	....	3845	1025	ac.	....	33	21.5	5.6	21.5	89	...
Oct. 25-26..	**C 19**	**2935**	....	ac.	....	**29**	**16.3**	**4.8**	**24.3**	**72**	...
Oct. 26-27..	**C 20**	**3710**	....	ac.	....	**33.6**	**13.3**	**5.0**	**31.0**	**106**	...
Oct. 27-28..	**C 21**	**4370**	....	ac.	....	**61**	**19.6**	**5.5**	**23.1**	**134**	...
Oct. 28-29..	**C 22**	**4035**	....	ac.	....	**61**	**19.4**	**5.4**	**22.9**	**107**	...
Oct. 29-30...	**C 23**	**3330**	....	ac.	....	**46**	**14.7**	**5.6**	**31.4**	**100**	...
Oct. 30-31..	**C 24**	**3765**	....	ac.	....	**47.8**	**16.3**	**5.0**	**25.3**	**93**	...
Nov. 7– 8....	....	3400	1029	....	+ + +	....	11.0	...	....	...	136

[1] Urine of 2 days combined and analyzed.

TABLE 51.—*Clinical chart—Case C.*

Diet.					Carbohydrate-balance.	$NaHCO_3$.	Naked body-weight.	Remarks.
Carbohydrate.	Protein.	Nitrogen.	Fat.	Alcohol.				
gms.	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*	
(?)	...	..	...	..	....	0	64.0	
70+	...	..	...	..	— 50	16	63.6	Strict diet and 300 gms. vegetables, 250 c. c. cream, 250 c. c. milk, 30 gms. bread, 18 gms. oatmeal, 150 gms. fruit.
100	...	..	...	..	— 80	24	....	
50	120	19	160	..	—100	24	65.3	The same as March 31. No bread.
50	...	..	...	..	— 65	24	....	Do.
60	113	18	200	..	— 45	20	66.5	
25	...	..	116	..	— 30	12	66.0	600 gms. vegetables, 250 c. c. cream ; vegetable day.
...	...	..	...	..	....	0	....	
30	...	..	200	..	— 20	0	64.9	450 gms. vegetables, 500 c. c. cream, 90 gms. butter, 4 yolks eggs, bacon ; vegetable day.
...	...	..	...	..	....	0	....	
50	...	..	...	..	....	0	64.4	300 gms. vegetables, 150 gms. fruit, 18 gms. oatmeal, 250 c.c. cream, 125 c.c. milk.
50	...	..	...	..	....	0	....	Do.
...	...	..	...	..	....	0	....	
...	...	..	...	..	....	**0**	....	
...	...	..	...	..	....	0	62.7	
...	...	..	...	..	....	**0**	....	
60	...	..	**175**	..	**— 65**	**0**	....	Strict diet and 250 c. c. cream, 250 c. c. thin cream, 18 gms. oatmeal, 150 gms. fruit, 600 gms. vegetables, 90 gms. butter.
60	...	..	**175**	..	**— 80**	**0**	....	Do.
60	...	..	175	..	— 65	0	....	Do.
...	...	..	...	..	....	..	....	
50	...	..	...	..	....	0	62.7	The same approximately.
50	...	..	...	..	....	12	63.4	
...	...	..	...	..	....	12	61.1	Vegetables, cream.
40	30	5	90	15	— 65	0	....	60 gms. oatmeal, 3 eggs, 90 gms. butter, 150 gms. wine.
100	60	10	155	15	+ 5	0	61.0	150 gms. oatmeal, 6 eggs, 150 gms. butter, 150 gms. wine, 30 gms. cream.
...	...	..	...	..	....	0?	....	
...	...	..	...	..	....	0?	....	
50	...	..	...	..	....	0?	....	500 c. c. cream, 120 gms. fruit, 18 gms. oatmeal. Strict diet.
...	...	..	...	..	....	**0**	....	
...	...	..	...	..	....	0	....	
...	...	..	...	..	....	0	....	
...	...	..	...	..	....	**0**	**60.0**	
...	...	..	...	..	....	0	....	
...	...	..	...	..	....	0	59.4	Sept. 12.
...	...	..	...	..	....	0	60.4	Sept. 19.
60+	...	..	...	15	....	0	60.4	30 gms. oatmeal, 250 c. c. cream, 600 gms. vegetables, 150 gms. fruit.
16+	70	11	175	15	....	0	59.4	180 gms. meat, 3 eggs, 250 c. c. cream, 100 gms. butter, 300 gms. vegetables, 30 gms. whiskey.
...	...	..	...	15	....	0	....	
...	...	..	...	15	....	0	....	
...	...	..	...	15	....	0	....	
...	...	..	...	15	....	0	....	
...	...	..	...	15	....	0	....	
15	...	..	**55**	**15**	**— 55**	**0**	**54.9**	Vegetables : Tomato, lettuce, cabbage, cucumber, celery ; butter 30 gms., oil 30 gms., broths, coffee.
98	**20**	**3**	**174**	**30**	**— 10**	**0**	....	Potato 450 gms., cream 250 c. c., butter 146 gms.
65	...	..	...	**30**	**— 70**	**60**	....	Strict diet, cream 250 c. c., milk 500 c. c., vegetables, 2 oranges. Improved wonderfully, upon taking sodium bicarbonate.
65	...	..	...	**30**	**— 40**	**60**	**56.1**	Do.
125	...	..	...	**30**	**+ 25**	**25**	....	Oatmeal 180 gms., cream 250 c. c., broths, coffee.
65	...	..	...	**22**	**— 30**	**25**	...	Diet as on Oct. 28 and 29.
40+	...	..	...	30	....	25	59.1	

however, was soon shown by the unassimilated carbohydrates in the diet and by the acidosis, and it was confirmed by the experiments with food in the calorimeter. The patient showed a minus carbohydrate-balance of over 50 grams upon a vegetable day, and only a positive carbohydrate-balance of 25 grams after the administration of 126 grams carbohydrate in the form of oatmeal. Upon this day there were 46 grams of β-oxybutyric acid in the urine. He continued to fail after leaving the hospital, and died on December 8, 1909, in coma. The history of the case is shown in table 51.

In considering the question as to the proper quantity of carbohydrates which a patient of this type should be given, we would call attention to what occurred in the case of I when carbohydrates in his diet were restricted from an indefinitely large quantity to even 100 grams. The symptoms of extreme acidosis appeared in this patient as promptly when taking 100 grams of carbohydrates as in other patients when the carbohydrates were restricted to 0.

Diet.—The treatment of this patient was the same as that of Cases A and B, but as the patient did not receive training at the hospital until long after he was first seen his diet was never as accurately controlled. The character of the diet was essentially the same as in the previous cases, A and B. The quantity of carbohydrates allowed varied from 100 grams to 50 grams, except for three periods. The attempt was made to keep the quantity of nitrogen in the diet about 15 to 20 grams, but it is obvious that this was frequently exceeded. A large quantity of fat was taken, but exactly how much is unknown. A vegetable day, given on May 10, with a diet of 600 grams of vegetables and 250 c. c. of cream, resulted in a minus carbohydrate-balance of about 30 grams. A second vegetable day in which, however, the quantity of vegetables was 450 grams and the cream 500 c. c., and in addition the yolks of four eggs, also showed a minus carbohydrate-balance of about 20 grams. A third vegetable day, August 3, showed 85 grams of sugar by the polariscope during the 24 hours, and a fourth vegetable day, October 26, 72 grams of sugar in the urine by Citron's test, giving a minus carbohydrate-balance of about 55 grams. These vegetable days show the progress in the severity of the disease.

Oatmeal days.—Several attempts were made to give the patients oatmeal days according to the suggestions of von Noorden. With this patient such days were always more or less of a failure because the patient was not especially fond of oatmeal. However, it will be seen that upon August 5 he took 100 grams of carbohydrates in the form of oatmeal, and that upon this day for the first time since March 23 there was a positive carbohydrate-balance of 5 grams. This exerted, however, no essential effect upon the acidosis, for the β-oxybutyric acid was found to be 15 grams. A third oatmeal day was given October 30, when 125 grams of carbohydrates in the form of oatmeal were eaten. Upon this day there was a positive carbohydrate balance of approximately 25 grams. The acidosis was distinctly not lessened, as will be seen from a study of the chart.

Potato day.—Upon October 27, 450 grams of potato were given, and 250 c. c. of cream. This potato, with the cream, was analyzed and found to contain 92 grams of carbohydrate. The analysis was as follows:

Weight of potato, moist	grams	450
Weight of potato, dry	do	106.9
Amount taken for analysis	do	11.372
Carbohydrates found	per cent	86
Total quantity of carbohydrates in 450 gms	grams	92

The result of the potato day showed a slight minus carbohydrate-balance, approximately 10 grams. The acidosis was not lowered, as shown by the β-oxybutyric acid and ammonia.

The analyses of the urine, as shown by the chart, furnished a very accurate picture of the course of the disease.

Volume of urine.—The greatest quantity of urine observed by the patient was 5000 c. c., but the highest quantity reached while under observation was 4500 c. c. upon the first day. The quantity was undoubtedly due to the excessive amount of sugar, namely, 302 grams. During June, when the patient was probably in as good condition as at any time during the course of observation, the quantity of urine was about 2000 c. c. At this time the sugar was in the neighborhood of 100 grams. The subsequent rise in the volume of the urine was due more to the increase in acidosis than to the greater amount of sugar to be excreted. Magnus-Levy [1] long ago pointed out that it was impossible for a diabetic patient to remove large quantities of acid, particularly β-oxybutyric acid, from the body, unless the urine was greatly increased in amount, because β-oxybutyric acid can only be excreted in dilute solutions. Bearing this in mind, it is interesting to note the increasing volume of the urine as the severity of the case advanced. Thus in the latter days of the period, during which the patient was under observation, the urine attained an amount almost equal to that at the start, although the amount of sugar present was decidedly less. Increasing quantities of urine without correspondingly increasing quantities of sugar must be considered an ominous sign.

Nitrogen.—The quantity of nitrogen, 34 grams, excreted the first day upon which the patient came under observation indicates the excessively albuminous diet of an untreated diabetic patient.

Specific gravity.—The specific gravity of the urine ranged between 1023 and 1050, reaching the higher point only upon a single day, August 10.

Albumen.—The albumen never exceeded a slight trace. The sediment showed no casts or pus or blood in March, 1909.

Acidosis.—Acidosis was absent when the patient first came under observation. This is a common experience in cases where patients have lived upon a diet with unrestricted carbohydrates. As soon as the carbohydrates in the diet were restricted to between 70 and 100 grams in the 24 hours, acidosis appeared. This was shown in various ways. (See table 52.)

[1] Magnus-Levy, Archiv f. exp. Path. u. Pharm., 1899, **42**, p. 199.

TABLE 52.—*Quantitative indications in the urine of acidosis—Case C.*

Date.	Diacetic acid.	B-oxy-butyric acid.	Ammonia.		Sugar.			Respiratory quotient.
			Total.	Per cent of total nitrogen.	Citron method.	Rotation.	Difference (+or—)	
1909.		*grams.*	*gms.*		*grams.*	*gms.*	*gms.*	
Apr. 3	....	....	3.0	10.0	180	152	—28	....
May 6	++	....	2.5	9.9	107	110	+ 3	....
May 14	0	5.7	2.0	9.2	115	....	....	0.75
June 4	+	14.2	....	....	....	70	....	....
June 7	+	....	3.6	....	96	81	—15	....
June 11	....	14.6	2.9	11.6	141	....	....	.69
June 14	....	[1]13.0	....	....	....	....	....	....
June 15	....	[1]13.0	....	....	122	....	....	.69
June 25	....	....	2.6	9.6	123	....	....	....
July 21	++	....	4.1	20.0	....	115	....	....
Aug. 3	++	15.3	....	....	....	85	....	....
Aug. 5	+++	[1]18.5	....	....	106	88	—18	....
Aug. 6	++	[1]18.5	....	....	95	74	—21	....
Aug. 8	....	[1]14.2	....	....	....	101	....	....
Aug. 9	....	[1]14.2	....	....	....	134	....	....
Aug. 10	+	[1]14.2	....	....	....	124	....	....
Aug. 24	+++	49.5	....	....	170	137	—33	....
Sept. 28	+++	24.2	5.0	23.5	114	117	+ 3	....
Oct. 21	....	[1]33	....	....	57	....	....	....
Oct. 23	....	[1]33	....	....	127	....	....	....
Oct. 24	....	[1]33	....	....	126	....	....	....
Oct. 25	....	[1]33	5.6	21.5	89	....	....	....
Oct. 26	....	29	4.8	24.3	72	....	....	.72
Oct. 27	....	33.6	5.0	31.0	106	....	....	....
Oct. 28	....	[1]61	5.5	23.1	134	....	....	....
Oct. 29	....	[1]61	5.4	22.9	107	....	....	.70
Oct. 30	....	46	5.6	31.4	100?	....	....	....
Oct. 31	....	47.8	5.0	25.3	93	....	....	....

[1] Urine for 2, 3, or 4 days combined and analyzed.

Reaction.—The reaction of the urine was acid throughout, except upon one day, April 9, when it was alkaline. The extent of the acidity was shown when, upon October 28 and 29, 60 grams of sodium bicarbonate were daily administered without changing the reaction.

Diacetic acid.—Diacetic acid was absent when the patient first came under observation, but the restriction of the carbohydrates was immediately followed by its appearance in large quantity. The recent work of Lüthje [1] calls attention to the fact that one can not estimate the quantity of acidosis present by the intensity or depth of color of the urine upon the addition of ferric chloride. A slight increase in the total acidosis shows at once by a most pronounced Gerhardt's reaction, so that any subsequent increase must escape detection. Upon September 5 and 10, diacetic acid was recorded absent, but it was invariably found upon all other dates when the test was applied. Occasionally the test was omitted when the ammonia was quantitatively determined.

[1] Lüthje, Die Therapie der Gegenwart, 1910, **51**, p. 13.

B-oxybutyric acid.—This showed a steady increase when one considers the case as a whole. On successive dates it rose from 5.7 grams in the middle of May to 14.2 grams upon June 4, and remained in that vicinity until August, when another rise occurred to 15.3 grams, and 18.5 grams, to fall a little later to 14.2 grams. Upon August 24, 49.5 grams β-oxybutyric acid were excreted. The exact cause for this is not manifest. However, from this time on the daily quantities voided were on the whole higher, and at no time did they fall below 24.2 grams. When a large quantity of sodium bicarbonate was given upon October 28 and 29 the β-oxybutyric acid rose to 61 grams in the 24 hours, an amount seldom exceeded except in coma. The patient was unable to continue the large doses of sodium bicarbonate, and presumably this accounts in part for the fall in quantity of β-oxybutyric acid excreted. On the other hand, it may have been that these very high amounts of acid represent the washing-out of the acid from the system.

Ammonia.—The amount of nitrogen which left the body in the form of ammonia was considerable. Like the other signs of acidosis it was low at the first observation, but rose with considerable steadiness up toward the end. The moderate restriction of carbohydrates was accompanied by an excretion of 3 grams of ammonia, which diminished with the administration of sodium bicarbonate to 2.5 and 2 grams, respectively. When the alkali was omitted the ammonia promptly increased, and never again reached such low quantities as before. Even upon the days when 60 grams of sodium bicarbonate were given the quantity of ammonia was 5.5 and 5.4 grams, respectively.

The ammonia-nitrogen-nitrogen ratio rose similarly from 10 per cent at the start to 20 per cent in July, 23 per cent in September, and in October reached on two occasions 31 per cent. When one considers that a large quantity of alkali was being taken at this time these percentages have added significance.

EXPERIMENTS WITH CASE C.

With this subject 11 metabolism experiments were made, one of which was with the bed calorimeter. In 9 of these the subject entered the calorimeter without breakfast, after a 12-hours' fast. The other two metabolism experiments were made after the ingestion of food. Fourteen respiration experiments were also made with this subject. The vital statistics were as follows:

Date of birth, September 24, 1879; height, 166 centimeters; range of naked body-weight, 54.9 to 65.4 kilograms.

METABOLISM EXPERIMENT NO. C 1.

Date, April 13, 1909. Naked body-weight, 65.4 kilograms.

This was the first experience of the subject inside of the respiration calorimeter and, indeed, the first experiment made with him of any kind. He came to the laboratory without breakfast, after a 12-hours' fast, and entered the chair calorimeter at 8 a. m. The experiment began at 9 a. m. and continued for four 1-hour periods, ending at 1 p. m. No water was taken by the subject, and he

used the telephone three times after the beginning of the first period. The subject said that while the experiment was monotonous, he did not find it tiresome. He did not suffer from headache but said he was slightly hungry. He thought that the illumination of the chamber was very satisfactory.

The stethoscope, pneumograph, and electrical-resistance thermometer were used in this experiment. The pulse-rate ranged from 62 to 80, and the respiration-rate from 15 to 21. The data regarding the metabolism and the average pulse- and respiration-rates are given in table 53, and the statistics of urine in table 54.

TABLE 53.—*Measurements of metabolism—Metabolism experiment No. C 1.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
April 13, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
9 to 10 a.m.	25.0	22.9	212	267	34.7	0.79	89	74	18
10 to 11 a.m.	23.9	24.3	203	284	32.4	.72	85	72	17
11 a.m. to 12 noon	24.7	23.8	210	278	29.7	.76	82	70	19
12 noon to 1 p.m.	23.7	23.3	201	272	28.7	.74	80	70	18
Total 4 hours [1]	97.3	94.3	206	275	125.5	....	[2]336	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.15 c. c.; oxygen absorbed per kilogram per minute, 4.20 c. c.; heat eliminated per kilogram per hour, 1.28 calories.
[2] Rectal body-temperature at beginning, 37.05° C.; at end, 36.95° C. Heat production for total 4 hours, 331 calories.

TABLE 54.—*Statistics of urine—Metabolism experiment No. C 1.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
April 13, 1909.	*c. c.*		*grams.*	*grams.*	
$6^h 00^m$ a.m. to $11^h 04^m$ a.m.	382	1.019	2.65	9.2	3.47
11 04 a.m. 1 04 p.m.	214	1.016	1.32	2.3	1.74

METABOLISM EXPERIMENT No. C. 2.

Date, May 14, 1909. Naked body-weight, 64 kilograms.

This experiment also followed a 12-hours' fast, and the subject came to the laboratory without breakfast. He entered the calorimeter chamber at $7^h 57^m$ a. m. and the experiment began at $8^h 42^m$ a. m., and continued for three 1-hour periods, and one period of $1^h 18^m$, ending at 1 p. m. As the water supply of the cooling system froze in the refrigeration room just previous to the last period, and the temperature conditions in the chamber were thus affected, the last period was extended until the defect was remedied and temperature equilibrium was again obtained. The subject used the telephone four times while he was in the chamber. On coming out of the apparatus he said that he had no special comments to make except that he did not find it so monotonous as in the preceding experiment, and noticed no fluctuations in the temperature.

The stethoscope, pneumograph, and electrical-resistance thermometer were used in this experiment, the range for the pulse-rate being from 65 to 78, and the respiration-rate from 18 to 21.

The metabolism measurements are given in table 55, also the average pulse- and respiration-rates. The statistics of urine are given in table 56.

TABLE 55.—*Measurements of metabolism—Metabolism experiment No. C 2.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
May 14, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
8h 42m a.m. to 9h 42m a.m.	25.1	23.7	213	277	31.9	0.77	84	72	20
9 42 a.m. 10 42 a.m.	23.6	24.8	200	289	31.3	.69	82	71	20
10 42 a.m. 11 42 a.m.	24.5	53.2	208	270	29.1	.76	173	70	19
11 42 a.m. 1 00 p.m.	31.2		204		40.1			72	19
Total 4 h. 18 min.[1]	104.4	101.7	206	276	132.4	....	[2]339	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.22 c. c.; oxygen absorbed per kilogram per minute, 4.31 c. c.; heat eliminated per kilogram per hour, 1.23 calories.
[2] Rectal body-temperature at beginning, 37.00° C.; at end, 37.13° C. Heat production for total 4 hours, 18 minutes, 347 calories.

TABLE 56.—*Statistics of urine—Metabolism experiment No. C 2.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
May 13–14, 1909.	*c. c.*		*grams.*	*grams.*	
6h 00m a.m. to 6h 00m p.m.......	1555	1.035	9.67	78.6	....
6 00 p.m. 6 00 a.m.......	874	1.034	8.23	36.9	....
May 14, 1909.					
6h 00m a.m. to 10h 44m a.m.......	183	1.032	2.12	6.1	2.88
10 44 a.m. 1 05 p.m.......	119	1.028	1.47	2.0	1.36

METABOLISM EXPERIMENT No. C 3.

Date, June 8, 1909. Naked body-weight, 62.7 kilograms.

The subject entered the respiration chamber, without breakfast, at 7h 28m a. m. and the experiment began at 8h 14m a. m., continuing for four 1-hour periods, ending at 12h 14m p. m. He drank no water during the time he was in the chamber, and telephoned five times, twice in the first period. Near the end of the second period he slept for a short time and was awakened by the observer. He said after the experiment was over that as he had retired later than usual the previous night and had risen early that morning he found it difficult to keep awake during the experiment, and the reading became monotonous. The temperature conditions throughout the experiment were very constant.

The stethoscope, pneumograph, and electrical-resistance thermometer were used in this experiment. The pulse-rate ranged from 59 to 78 and the respiration-rate from 17 to 20. The data regarding the metabolism measurements and

the average pulse- and respiration-rates are given in table 57. The statistics of urine are given in table 58.

TABLE 57.—*Measurements of metabolism—Metabolism experiment No. C 3.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
June 8, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
8h 14m a.m. to 9h 14m a.m.	24.1	27.3	204	319	25.5	0.64	80	72	19
9 14 a.m. 10 14 a.m.	23.7	27.0	201	315	25.0	.64	76	71	[1]18
10 14 a.m. 11 14 a.m.	22.4	25.0	190	292	24.9	.65	78	64	18
11 14 a.m. 12 14 p.m.	22.5	22.2	191	259	25.3	.74	77	64	18
Total 4 hours [2].....	92.7	101.5	197	296	100.7	....	[3]311	..	..

[1] Records taken from 9h 48 a. m. to 10h 08m a. m.
[2] Carbon dioxide eliminated per kilogram per minute, 3.14 c. c.; oxygen absorbed per kilogram per minute, 4.72 c. c.; heat eliminated per kilogram per hour, 1.24 calories.
[3] Rectal body-temperature at beginning, 36.64° C.; at end, 36.82° C. Heat production for total 4 hours, 321 calories.

TABLE 58.—*Statistics of urine—Metabolism experiment No. C 3.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Ammonia.	Per cent total N as NH_3—N.	Sugar.	D : N.
June 7–8, 1909.	*c. c.*		*grams.*	*grams.*		*grams.*	
6h 00m a.m. to 6h 00m p.m.	822	1.039	5.30	0.79	12.3	59.4	....
6 00 p.m. 5 45 a.m.	912	1.037	7.86	1.30	13.6	45.1	....
June 8, 1909.							
5h 45m a.m. to 9h 12m a.m.	171	1.041	1.18	.26	17.8	14.6	12.37
9 12 a.m. 10 12 a.m.	80	1.040	.62	.13	17.7	5.8	9.36
10 12 a.m. 11 12 a.m.	48	1.042	.43	.11	20.9	3.7	8.61
11 12 a.m. 12 12 p.m.	42	1.043	.44	.11	20.4	3.0	6.82

METABOLISM EXPERIMENT NO. C 4.

Date, June 11, 1909. Naked body-weight, 63.1 kilograms.

The subject came to the laboratory as usual, without breakfast, and entered the calorimeter chamber at 7h 30m a. m. The experiment began at 8h 16m a. m., and continued for three 1-hour periods, ending at 11h 16m a. m. No water was taken and the subject telephoned three times, twice in the last period. No comments were made by the subject and the experiment appeared to be without incident. The temperature conditions were fairly constant throughout all of the periods.

The stethoscope, pneumograph, and electrical-resistance thermometer were used in this experiment, as previously. The range in the pulse-rate was from 62 to 73 and the respiration-rate from 17 to 21. The data regarding the measurement of the metabolism will be found in table 59, and the statistics of the urine in table 60.

TABLE 59.—*Measurements of metabolism—Metabolism experiment No. C 4.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
June 11, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$8^h 16^m$ a.m. to $9^h 16^m$ a.m.	24.7	26.0	210	303	36.7	0.69	82	67	20
9 16 a.m. 10 16 a.m.	23.7	....	201	...	33.2	....	83	67	20
10 16 a.m. 11 16 a.m.	23.5	....	199	...	32.6	....	77	66	20
Total 3 hours[1].....	71.9	....	203	303	102.5	....	[2]242	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.22 c. c.; oxygen absorbed per kilogram per minute from $8^h 16^m$ a. m. to $9^h 16^m$ a. m., 4.80 c. c.; heat eliminated per kilogram per hour, 1.28 calories.
[2] Rectal body-temperature at beginning 36.71° C.; at end 36.73° C. Heat production for total 3 hours, 244 calories.

TABLE 60.—*Statistics of urine—Metabolism experiment No. C 4.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Ammonia.	Per cent total N as NH_3—N.	Sugar.	D : N.
June 10–11, 1909.	*c. c.*		*grams.*	*grams.*		*grams.*	
$6^h 00^m$ a.m. to $6^h 00^m$ p.m.	930	1.041	8.45	1.06	10.3	69.2	....
6 00 p.m. 6 00 a.m.	1375	1.034	12.16	1.49	10.1	71.8	....
June 11, 1909.							
$6^h 00^m$ a.m. to $8^h 16^m$ a.m.	240	1.033	2.49	.34	11.2	11.7	4.70
8 16 a.m. 10 16 a.m.	115	1.028	1.10	.15	10.9	4.4	4.00
10 16 a.m. 11 16 a.m.	162	1.029	1.75	.23	10.9	5.2	2.97
11 16 a.m. 12 16 p.m.	114	1.019	1.00	.12	10.0	1.8	1.80

METABOLISM EXPERIMENT No. C 5.

Date, June 15, 1909. Naked body-weight, 62.6 kilograms.

The subject came to the laboratory as in previous experiments, without eating breakfast, and entered the calorimeter chamber at $8^h 54^m$ a. m. The experiment began at $9^h 30^m$ a. m., and continued for three 1-hour periods, ending at $12^h 30^m$ p. m. He telephoned three times during the experiment, twice during the first

TABLE 61.—*Measurements of metabolism—Metabolism experiment No. C 5.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
June 15, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$9^h 30^m$ a.m. to $10^h 30^m$ a.m.	24.3	26.6	206	310	36.1	0.66	91	74	19
10 30 a.m. 11 30 a.m.	22.5	21.9	191	256	35.2	.75	85	70	20
11 30 a.m. 12 30 p.m.	22.9	24.8	194	289	30.3	.67	79	71	20
Total 3 hours[1].....	69.7	73.3	197	285	101.6	....	[2]255	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.15 c. c.; oxygen absorbed per kilogram per minute, 4.55 c. c.; heat eliminated per kilogram per hour, 1.36 calories.
[2] Rectal body-temperature at beginning, 36.91° C.; at end, 36.84° C. Heat production for total 3 hours, 252 calories.

period. No water was taken by the subject, and he made no comments regarding the experiment. The temperature conditions were fairly constant in all periods.

The pulse- and respiration-rates were measured in the usual way, and the body-temperature was measured with the electrical-resistance thermometer. The range for the pulse-rate was from 62 to 78, and the respiration-rate from 16 to 25. The data for the metabolism measurements and the average pulse- and respiration-rates will be found in table 61, and the statistics of the urine in table 62.

TABLE 62.—*Statistics of urine—Metabolism experiment No. C 5.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
June 14–15, 1909.	*c. c.*		*grams.*	*grams.*	
$6^h 00^m$ a.m. to $6^h 00^m$ p.m.	960	1.036	10.96	57.9	....
6 00 p.m. 6 00 a.m.	1440	1.036	11.21	105.4	....
June 15, 1909.					
$6^h 00^m$ a.m. to $9^h 30^m$ a.m.	96	1.038	.62	7.0	11.29
9 30 a.m. 11 30 a.m.	169	1.041	1.37	13.1	9.56
11 30 a.m. 12 30 p.m.	52	1.044	.55	4.1	7.45

METABOLISM EXPERIMENT No. C 6.

Date, June 18, 1909. Naked body-weight, 62.7 kilograms.

The subject came to the laboratory without breakfast and entered the respiration chamber at $8^h 45^m$ a. m. The experiment began at $9^h 32^m$ a. m. and continued for three 1-hour periods, ending at $12^h 32^m$ p. m. No water was taken during this time and the subject telephoned only once, just after the beginning of the second period. The temperature conditions in the chamber were satisfactory. No comments were made by the subject regarding the experiment.

The measurements of pulse-rate, respiration-rate, and body-temperature were made in the usual way, the pulse-rate ranging from 61 to 71, and the respiration-rate from 19 to 25. The data for the metabolism measurements and the average pulse- and respiration-rates are given in table 63, and the statistics of urine in table 64.

TABLE 63.—*Measurements of metabolism—Metabolism experiment No. C 6.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
June 18, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$9^h 32^m$ a.m. to $10^h 32^m$ a.m.	21.9	21.6	186	252	31.9	0.74	86	66	[1]21
10 32 a.m. 11 32 a.m.	22.8	22.0	193	257	27.0	.75	76	67	24
11 32 a.m. 12 32 p.m.	22.5	22.1	191	258	29.1	.74	75	66	[2]19
Total 3 hours[3]	67.2	65.7	190	256	88.0	....	[4]237	..	..

[1] One record at $9^h 59^m$ a. m.
[2] One record at $11^h 49^m$ a. m.
[3] Carbon dioxide eliminated per kilogram per minute, 3.03 c. c.; oxygen absorbed per kilogram per minute, 4.08 c. c.; heat eliminated per kilogram per hour, 1.26 calories.
[4] Rectal body-temperature at beginning, 36.55° C.; at end, 36.72° C. Heat production for total 3 hours, 248 calories.

TABLE 64.—*Statistics of urine—Metabolism experiment No. C 6.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Ammonia.	Per cent total N as NH_3—N.	Sugar.	D : N.
June 17–18, 1909.	c. c.		grams.	grams.		grams.	
7h 15m a.m. to 7h 15m p.m.	720	1.043	7.03	1.12	13.1	61.7	....
7 15 p.m. 5 40 a.m.	845	1.039	8.98	1.28	11.7	53.9	....
June 18, 1909.							
5h 40m a.m. to 7h 20m a.m.	117	1.038	1.20	.22	15.0	7.1	5.92
7 20 a.m. 10 32 a.m.	190	1.037	2.41	.41	14.1	10.5	4.36
10 32 a.m. 12 32 p.m.	94	1.035	1.32	.23	14.4	3.6	2.73

METABOLISM EXPERIMENT No. C 7.

Date, June 22, 1909. Naked body-weight, 62.8 kilograms.

The subject entered the chair calorimeter, without breakfast, at about 7h 45m a. m., and the experiment began at 8h 43m a. m. The measurements were made in two periods, the first 1 hour in length and the second 1½ hours long. The experiment ended at 11h 13m a. m. The subject drank no water and telephoned once just after the beginning of the experiment.

The measurements of the pulse and respiration were made in the usual manner, the range in pulse-rate being from 51 to 69, and the respiration-rate from 16 to 22.

The measurements of the metabolism and the average respiration- and pulse-rates are given in table 65, and the statistics of the urine in table 66.

TABLE 65.—*Measurements of metabolism—Metabolism experiment No. C 7.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
June 22, 1909.	gms.	gms.	c. c.	c. c.	gms.		cals.		
8h 43m a.m. to 9h 43m a.m.	24.4	25.0	207	292	29.4	0.71	90	65	19
9 43 a.m. 11 13 a.m.	33.7	34.2	191	266	38.1	.72	130	63	20
Total 2 h. 30 min.[1] . .	58.1	59.2	197	276	67.5	....	[2]220	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.14 c. c.; oxygen absorbed per kilogram per minute, 4.40 c. c.; heat eliminated per kilogram per hour, 1.40 calories.
[2] Rectal body temperature at beginning, 36.62° C.; at end, 36.84° C. Heat production for total 2 hours, 30 minutes, 233 calories.

TABLE 66.—*Statistics of urine—Metabolism experiment No. C 7.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Ammonia.	Per cent total N as NH_3—N.	Sugar.	D : N.
June 21–22, 1909.	c. c.		grams.	grams.		grams.	
5h 00m a.m. to 5h 00m p.m.	900	1.035	4.91	.69	11.6	65.5	....
5 00 p.m. 5 00 a.m.	1146	1.037	9.38	1.36	11.9	76.2	....
5 00 a.m. 7 20 a.m.	135	1.041	1.17	.18	12.8	10.5	8.97
7 20 a.m. 8 43 a.m.	105	1.038	1.03	.17	13.6	7.4	7.19
8 43 a.m. 11 13 a.m.	176	1.039	1.92	.33	14.1	11.5	5.99

METABOLISM EXPERIMENT No. C 8.

Date, June 25, 1909. Naked body-weight, 62.4 kilograms.

This experiment was made with the bed calorimeter and the subject entered the chamber at $10^h 10^m$ a. m. The experiment began at $10^h 53^m$ a. m. and continued for two 1-hour periods, ending at $12^h 53^m$ p. m.

The pulse- and respiration-rates and the measurements of the body-temperature were taken in the usual way, the range in pulse-rate being from 58 to 72, and the respiration-rate from 18 to 21. The metabolism measurements and the average pulse- and respiration-rates are given in table 67. As the measurement of the heat-elimination was defective, these measurements are not included in the table. The statistics of the urine are given in table 68.

TABLE 67.—*Measurements of metabolism—Metabolism experiment No. C 8.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.				
June 25, 1909.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*			
$10^h 53^m$ a.m. to $11^h 53^m$ a.m.	21.8	21.9	185	256	27.9	0.72	65	20
11 53 a.m. 12 53 p.m.	21.6	22.5	183	263	33.9	.70	63	19
Total 2 hours [1]	43.4	44.4	184	259	61.8	....	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 2.95 c. c.; oxygen absorbed per kilogram per minute, 4.15 c. c.

TABLE 68.—*Statistics of urine—Metabolism experiment No. C 8.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Ammonia.	Per cent total N as NH_3—N.	Sugar.	D : N.
June 24–25, 1909.	*c. c.*		*grams.*	*grams.*		*grams.*	
$5^h 45^m$ a.m. to $5^h 45^m$ p.m.	775	1.036	10.19	1.62	13.0	35.6	....
5 45 p.m. 5 45 a.m.	1238	1.037	11.23	1.49	10.9	81.3	....
5 45 a.m. 10 00 a.m.	332	1.034	3.24	.59	15.1	17.2	5.31
10 00 a.m. 10 53 a.m.	62	1.031	.69	.12	14.5	2.5	3.62
10 53 a.m. 1 00 p.m.	123	1.029	1.35	.26	15.6	4.3	3.19

METABOLISM EXPERIMENT No. C 9.

Date, October 26, 1909. Naked body-weight, 54.9 kilograms.

This experiment was made with the chair calorimeter and differed slightly from the preceding experiments in that the subject ate a small spoonful of oatmeal before entering the chamber and drank a glassful of cold water. He entered the chamber at $9^h 36^m$ a. m. and the experiment began at $10^h 26^m$ a. m., and continued for two 1-hour periods, ending at $12^h 26^m$ p. m. During the experiment he drank 50 c. c. of water and telephoned once in the first period and twice in the second. The subject was reading during the experiment and was very quiet in both periods. He said that he was very comfortable, with the exception of a slight irritation caused by the rectal thermometer. The temperature conditions in the apparatus were good throughout the experiment.

The measurements of pulse-rate, respiration-rate, and body-temperature were made in the usual way, the range in pulse-rate being from 77 to 86, and the respiration-rate from 17 to 19. The measurements of the metabolism and the average pulse- and respiration-rates are given in table 69, and the statistics of urine in table 73.

TABLE 69.—*Measurements of metabolism—Metabolism experiment No. C 9.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
October 26, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$10^h 26^m$ a.m. to $11^h 26^m$ a.m.	22.1	19.3	187	225	28.4	0.83	67	83	18
11 26 a.m. 12 26 p.m.	19.9	23.3	169	272	31.6	.62	71	82	19
Total 2 hours [1].....	42.0	42.6	178	249	60.0	....	[2]138	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.24 c. c.; oxygen absorbed per kilogram per minute, 4.54 c. c.; heat eliminated per kilogram per hour, 1.26 calories.
[2] Rectal body-temperature at beginning, 37.04° C.; at end, 37.32° C. Heat production for total 2 hours, 153 calories.

METABOLISM EXPERIMENT No. C 10.

Date, May 27, 1909. Naked body-weight, 64.7 kilograms.

This experiment differed from those preceding in that the subject took food. He entered the chair calorimeter at $7^h 33^m$ a. m. and began eating broiled beefsteak, part tenderloin, at $7^h 43^m$ a. m., finishing at $8^h 04^m$ a. m. In all 253 grams free from fat were eaten. The experiment began at $8^h 48^m$ a. m., continuing for four 1-hour periods, ending at $12^h 48^m$ p. m. No water was taken by the subject and he telephoned five times during the experiment, twice in the first period. The subject said that he found it difficult to urinate as often as was requested, and while the experiment did not weary him he found it somewhat tedious.

TABLE 70.—*Measurements of metabolism—Metabolism experiment No. C 10.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
May 27, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$8^h 48^m$ a.m. to $9^h 48^m$ a.m.	26.6	27.8	226	324	31.1	0.69	88	71	19
9 48 a.m. 10 48 a.m.	26.6	27.0	226	315	31.7	.71	84	73	20
10 48 a.m. 11 48 a.m.	26.5	26.9	225	314	29.6	.71	84	71	20
11 48 a.m. 12 48 p.m.	25.9	26.0	220	303	31.4	.72	81	68	19
Total 4 hours [1].....	105.6	107.7	224	314	123.8	....	[2]337	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.46 c. c.; oxygen absorbed per kilogram per minute, 4.85 c. c.; heat eliminated per kilogram per hour, 1.30 calories.
[2] Rectal body-temperature at beginning, 37.23° C.; at end, 37.47° C. Heat production for total 4 hours, 351 calories.

The stethoscope, pneumograph, and electrical-resistance thermometer were all used in this experiment, the pulse-rate ranging from 62 to 78, and the respiration-rate from 16 to 22. The measurements of the metabolism, also the average pulse- and respiration-rates, will be found in table 70, and the statistics of urine in table 71.

TABLE 71.—*Statistics of urine—Metabolism experiment No. C 10.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
May 26–27, 1909.	*c. c.*		*grams.*	*grams.*
6h 00m a.m. to 6h 00m p.m.	925	1.033	7.75	44.4
6 00 p.m. 6 00 a.m.	945	1.036	11.19	44.6
May 27, 1909.				
6h 00m a.m. to 7h 30m a.m.	153	1.032	1.55	5.9
7 30 a.m. 8 48 a.m.	174	1.028	1.51	5.8
8 48 a.m. 9 48 a.m.	160	1.027	1.22	4.9
9 48 a.m. 10 48 a.m.	100	1.027	.91	2.8
10 48 a.m. 11 48 a.m.	106	1.029	1.14	3.1
11 48 a.m. 1 15 p.m.	109	1.030	1.34	3.2

METABOLISM EXPERIMENT No. C 11.

Date, October 29, 1909. Naked body-weight, 56.1 kilograms.

In this, as in the preceding experiment, the subject took food. He entered the chair calorimeter at 10h 06m a. m., and between 10h 14m a. m. and 10h 28m a. m. he ate 545 grams of cooked oatmeal (60 grams of carbohydrates). The cereal was very warm when eaten, and although the cream was provided the subject used none. The subject drank 155 c. c. of water with the food, and said that he found it difficult to eat all of the oatmeal. The experiment began at 11h 01m a. m. and continued for two 1-hour periods, ending at 1h 01m p. m. During the experiment he drank 56 c. c. of water at 11h 04m a. m. and telephoned at 11h 02m a. m., and again at 12h 02m p. m.

The pulse-rate, respiration-rate, body-temperature, and muscular activity were measured in the usual manner, the pulse-rate ranging from 59 to 69, and the respiration-rate from 14 to 18. The subject was very quiet during the first pe-

TABLE 72.—*Measurements of metabolism—Metabolism experiment No. C 11.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
October 29, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
11h 01m a.m. to 12h 01m p.m.	19.7	21.8	167	254	27.3	0.66	74	62	17
12 01 p.m. 1 01 p.m.	21.5	21.3	182	249	27.9	.74	72	62	16
Total 2 hours [1]	41.2	43.1	175	251	55.2	....	[2]146	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.12 c. c.; oxygen absorbed per kilogram per minute, 4.47 c. c.; heat eliminated per kilogram per hour, 1.30 calories.
[2] Rectal body-temperature at beginning, 37.20° C.; at end, 37.06° C. Heat production for total 2 hours, 140 calories.

riod. The measurements of the metabolism and the average pulse- and respiration-rates are shown in table 72, and the statistics of urine in table 73.

TABLE 73.—*Statistics of urine—Case C, Oct. 24-31, 1909.*

Experiment No.	Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
	October 24–25, 1909.	c. c.		grams.	grams.	
	7^h00^m a.m. to 4^h00^m p.m. .	1150	....	7.05	39.4	....
	4 00 p.m. 7 00 a.m. .	2695	....	11.02	73.0	....
	October 25–26, 1909.					
C 19	7^h00^m a.m. to 9^h45^m a.m. .	505	....	2.31	12.7	5.50
	9 45 a.m. 10 30 a.m. .	100	....	.59	2.8	....
	10 30 a.m. 1 45 p.m. .	295	....	1.88	8.7	....
	1 45 p.m. 5 30 p.m. .	550	....	2.95	16.4	....
	5 30 p.m. 7 00 p.m. .	260	....	1.35	5.8	....
	7 00 p.m. 9 00 p.m. .	247	....	1.44	5.5	....
	9 00 p.m. 6 00 a.m. .	860	....	4.90	18.6	....
	6 00 a.m. 7 00 a.m. .	118	....	.58	1.9	....
	October 26–27, 1909.					
C 20	7^h00^m a.m. to 9^h31^m a.m. .	297	1.018?	1.16	4.9	4.22
	9 31 a.m. 10 28 a.m. .	170	1.017?	.59	2.8	4.75
C 9	10 28 a.m. 11 28 a.m. .	173	1.018?	.57	3.4	5.97
	11 28 a.m. 12 28 p.m. .	140	....	.54	3.2	5.93
	12 28 p.m. 4 40 p.m. .	495	1.021	1.97	13.2	....
	4 40 p.m. 8 40 p.m. .	785	1.024	2.28	32.0	....
	8 40 p.m. 3 20 a.m. .	1029	1.023	3.25	30.3	....
	3 20 a.m. 6 45 a.m. .	514	1.023	1.67	15.3	....
	6 45 a.m. 7 15 a.m. .	105	1.027	.42	3.7	....
	October 27–28, 1909.					
C 21	7^h15^m a.m. to 9^h55^m a.m. .	327	1.021	.98	9.9	10.10
	9 55 a.m. 11 45 a.m. .	230	1.024	.84	8.2	....
	11 45 a.m. 1 20 p.m. .	458	1.024	1.48	16.3	....
	1 20 p.m. 5 15 p.m. .	463	1.027	2.26	16.9	....
	5 15 p.m. 9 30 p.m. .	747	1.026	3.72	25.5	....
	9 30 p.m. 2 45 a.m. .	1284	1.025	4.99	41.6	....
	2 45 a.m. 7 10 a.m. .	862	1.027	4.04	25.1	....
	October 28–29, 1909.					
C 22	7^h10^m a.m. to 9^h25^m a.m. .	241	1.023	1.33	5.9	4.44
	9 25 a.m. 10 09 a.m. .	220	....	.60	2.9	4.83
	10 09 a.m. 2 15 p.m. .	718	1.026	3.35	23.9	....
	2 15 p.m. 6 10 p.m. .	634	1.024	3.26	19.7	....
	6 10 p.m. 9 15 p.m. .	466	1.024	2.28	14.6	....
	9 15 p.m. 10 15 p.m. .	120	1.029	.65	3.2	....
	10 15 p.m. 3 15 a.m. .	1173	1.024	4.70	32.6	....
	3 15 a.m. 7 00 a.m. .	563	1.018?	2.58	13.5	....
	October 29–30, 1909.					
C 23	7^h00^m a.m. to 10^h00^m a.m. .	360	1.023	1.78	7.5	4.21
	10 00 a.m. 11 04 a.m. .	178	1.026	.81	5.5	....
C 11	11 04 a.m. 12 04 p.m. .	185	1.030	.62	8.3	....
	12 04 p.m. 1 04 p.m. .	152	1.029	.58	6.9	....
	1 04 p.m. 4 00 p.m. .	408	1.032	1.78	18.8	....
	4 00 p.m. 6 15 p.m. .	728	1.028	2.86	29.4	....
	6 15 p.m. 10 20 p.m. .	294	1.028	1.27	9.8	....
	10 20 p.m. 7 10 a.m. .	1023	1.021	4.17	18.7	....
	October 30–31, 1909.					
C 24	7^h10^m a.m. to 10^h15^m a.m. .	340	1.023	1.35	6.8	5.04
	10 15 a.m. 12 30 p.m. .	254	1.027	.96	8.4	....
	12 30 p.m. 1 30 p.m. .	163	1.028	.56	6.9	....
	1 30 p.m. 6 15 p.m. .	658	1.028	2.55	19.8	....
	6 15 p.m. 8 30 p.m. .	502	1.026	2.03	14.3	....
	8 30 p.m. 5 45 a.m. .	1290	1.021	5.15	27.3	....
	5 45 a.m. 7 00 a.m. .	222	1.025	1.11	5.1	....
	7 00 a.m. 9 55 a.m. .	334	1.023	1.65	4.3	2.61

A comparison of the metabolism experiments with Case C is given in table 74.

TABLE 74.—*Comparison of metabolism experiments with Case C.*

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Respiratory quotient.	Heat eliminated per hour.	Heat produced per hour.	Average pulse per minute.	Average respiration per minute.
EXPERIMENTS WITHOUT FOOD.										
	1909.	*kilos.*	*hrs.*	*c. c.*	*c. c.*		*cals*	*cals.*		
C 1	Apr. 13	65.4	4	206	275	0.75	84	83	72	18.0
C 2	May 14	64.0	4⅓	206	276	.75	79	81	71	19.5
C 3	June 8	62.7	4	197	296	.67	78	80	68	18.5
C 4	June 11	63.1	3	203	303	.69	81	81	67	20.0
C 5	June 15	62.6	3	197	285	.69	85	84	72	20.0
C 6	June 18	62.7	3	190	256	.74	79	83	66	21.5
C 7	June 22	62.8	2½	197	276	.71	88	93	64	19.5
C 8	June 25 [1]	62.4	2	184	259	.71	..	..	64	19.5
C 9	Oct. 26 [2]	54.9	2	178	249	.72	69	77	83	18.5
EXPERIMENTS WITH FOOD.										
	1909.									
C 10	May 27 [3]	64.7	4	224	314	0.71	84	88	71	19.5
C 11	Oct. 29 [4]	56.1	2	175	251	.70	73	70	62	16.5

[1] Bed calorimeter.
[2] 39 minutes before the experiment began, the subject finished eating one teaspoonful of oatmeal.
[3] 44 minutes before the experiment began, the subject finished eating 253 grams of cooked beefsteak.
[4] 33 minutes before the experiment began, the subject finished eating 545 grams of oatmeal.

RESPIRATION EXPERIMENT No. C 12.

Date, June 11, 1909. Naked body-weight, 63.1 kilograms.

As the respiratory quotient in the metabolism experiment of this date appeared to be unusually low, it was decided to shorten the experiment and make the measurements in two 1-hour periods instead of the four originally planned. The subject was then immediately transferred to the respiration apparatus. This was the first time the apparatus had been used for this subject. Two separate periods were included in the experiment, 10 and 15 minutes in length, respectively. In the second period, the subject said that he found it slightly more difficult to breathe into the system than into the room air. The temperature conditions were fairly constant, and the results appeared to be satisfactory. The data for this experiment will be found in table 75.

TABLE 75.—*Results of respiration experiment No. C 12.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
June 11, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
11h 33m a.m.	10	1	186	262	0.71	64	15
11 49 a.m.	15	3	165	244	.68	63	14
Average			[1]176	[1]253	0.70	64	15

[1] Carbon dioxide eliminated per kilogram per minute, 2.79 c. c.; oxygen absorbed per kilogram per minute, 4.01 c. c.

RESPIRATION EXPERIMENT No. C 13.

Date, June 15, 1909. Naked body-weight, 62.6 kilograms.

Inasmuch as the respiratory quotient in the preceding metabolism experiments had been considerably lower than would be expected, it was decided to make a respiration experiment with this subject before he entered the calorimeter. Four separate periods were included in the experiment, the first 10 minutes in length, and the last three 15 minutes each. The intermission between the separate periods was from 10 to 15 minutes in length. Previous to the first period, the subject lay upon the couch for some 12 minutes, and was more or less active during this time. After the first period, and preceding the second, he was talking with the physician in attendance. The results of the experiment are given in table 76.

TABLE 76.—*Results of respiration experiment No. C 13.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
June 15, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
7h 35m a.m.	10	5	165	....	....	76	16
7 54 a.m.	15	4	181	284	0.64	71	16
8 17 a.m.	15	..	179	281	.64	73	15
8 39 a.m.	15	3	171	270	.63	74	16
Average			[1]174	[1]278	0.64	73	16

[1] Carbon dioxide eliminated per kilogram per minute, 2.78 c. c.; oxygen absorbed per kilogram per minute, 4.44 c. c.

RESPIRATION EXPERIMENT No. C 14.

Date, June 18, 1909. Naked body-weight, 62.7 kilograms.

This respiration experiment preceded the metabolism experiment of the same date and included four periods, the first one of 10 minutes and the last three of 15 minutes each. The time between periods was less than 10 minutes in all cases. The results of the experiment are found in table 77.

TABLE 77.—*Results of respiration experiment No. C 14.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
June 18, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
7h 29m a.m.	9	55	199	263	0.76	63	15
7 48 a.m.	15	2	164	246	.66	59	17
8 10 a.m.	15	2	164	245	.67	66	16
8 32 a.m.	15	2	197	269	.73	66	16
Average			[1]181	[1]256	0.71	64	16

[1] Carbon dioxide eliminated per kilogram per minute, 2.89 c. c.; oxygen absorbed per kilogram per minute, 4.08 c. c.

RESPIRATION EXPERIMENT No. C 15.

Date, June 22, 1909. Naked body-weight, 62.8 kilograms.

This experiment followed immediately after the metabolism experiment of the same day, and included four separate periods, the first 10 minutes in length and the last three 15 minutes long. The time between the periods was less than 10 minutes in all cases. In the second period there appeared to be a leak around the nose, and the subject said that the nosepiece in the right nostril was loose. The results of the experiment are given in table 78.

TABLE 78.—*Results of respiration experiment No. C 15.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
June 22, 1909	*m.*	*s.*	*c. c.*	*c. c.*			
11h 30m a.m.	10	4	168	249	0.68	64	15
12 08 p.m.	15	1	158	234	.68	60	15
12 28 p.m.	15	4	162	238	.68	64	15
Average			[1]163	[1]240	0.68	63	15

[1] Carbon dioxide eliminated per kilogram per minute, 2.60 c. c.; oxygen absorbed per kilogram per minute, 3.82 c. c.

RESPIRATION EXPERIMENT No. C 16.

Date, June 25, 1909. Naked body-weight, 62.4 kilograms.

This respiration experiment immediately preceded the metabolism experiment of the same date and included seven separate periods, all 15 minutes in length, with the exception of the first period, which was 10 minutes long. The intermission between the fifth and sixth periods was longer than usual, being 36 minutes. The results of the experiment are given in table 79.

TABLE 79.—*Results of respiration experiment No. C 16.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
June 25, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
7h 27m a.m.	10	1	163	253	0.64	65	19
7 42 a.m.	15	0	170	262	.65	60	17
8 05 a.m.	15	0	177	261	.68	62	17
8 25 a.m.	15	2	191	272	.70	69	15
8 46 a.m.	15	3	177	268	.66	72	15
9 22 a.m.	15	4	....	274	....	67	15
9 44 a.m.	15	1	177	260	.68	64	16
Average			[1]176	[1]264	0.67	66	16

[1] Carbon dioxide eliminated per kilogram per minute, 2.82 c. c.; oxygen absorbed per kilogram per minute, 4.23 c. c.

RESPIRATION EXPERIMENT No. C 17.

Date, August 9, 1909. Naked body-weight, 61 kilograms.

Some 20 minutes previous to this experiment, the subject ate some oatmeal which, before cooking, weighed 60 grams. Only one period was included, 14 minutes in length. The results are as follows: Carbon dioxide, 208 c. c. per minute; oxygen, 310 c. c. per minute; respiratory quotient, 0.67; average pulse per minute, 73, and average respirations per minute, 17.

RESPIRATION EXPERIMENT No. C 18.

Date, August 24, 1909. Naked body-weight, 60 kilograms.

This and the subsequent respiration experiments were without food unless otherwise stated.

The experiment on this day included five separate periods, the first period 10 minutes in length, and the last four each 15 minutes long. The intermission between periods was a little longer than usual. During the first period, the

TABLE 80.—*Results of respiration experiment No. C 18.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
August 24, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
7h 38m a.m.	10	..	161	230	0.70	61	17
8 00 a.m.	15	..	173	233	.75	58	16
8 26 a.m.	14	30	177	242	.73	69	14
8 46 a.m.	15	..	176	251	.70	69	15
9 07 a.m.	14	30	149	224	.67	63	16
Average			[1]167	[1]236	0.71	64	16

[1] Carbon dioxide eliminated per kilogram per minute, 2.78 c. c.; oxygen absorbed per kilogram per minute, 3.93 c. c.

subject was inclined to be sleepy. After the second period he made a slight change in the adjustment of the nosepiece in the right nostril, as he said that it was pushed in so far that it was uncomfortable. This did not apparently affect the closure, which seemed to be perfect. Previous to the third period the physician in attendance talked with the subject for a few minutes, evidently affecting the pulse-rate, which rose from 58 to 69. At the end of the fifth period the subject was sound asleep. The results during the different periods were variable, but this does not seem to be due to experimental conditions. The data are given in table 80.

RESPIRATION EXPERIMENT No. C 19.

Date, October 25, 1909. Naked body-weight, 54.9 kilograms.

The experiment on this date included four periods of the usual lengths and with the usual intermissions. Surgeon's plaster was used to obtain a perfect closure of the mouth. The subject had a cold-sore in the left nostril but this did not appear to affect the closure with the nosepieces. During the first period the oxygen supply diminished, and this seemed to increase the respiration-rate, but when a new cylinder of oxygen was substituted it became perfectly normal again. Between the first and second periods the nosepiece in the left nostril was released, but there was no change in the adjustment at any other time during the experiment. The results are given in table 81.

TABLE 81.—*Results of respiration experiment No. C 19.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
October 25, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
8h 18m a.m.	9	43	216	308	0.70	73	16
8 38 a.m.	15	13	176	253	.70	73	15
9 02 a.m.	15	13	165	244	.68	73	15
9 25 a.m.	15	..	176	260	.68	72	15
Average			[1]183	[1]266	0.69	73	15

[1] Carbon dioxide eliminated per kilogram per minute, 3.33 c. c.; oxygen absorbed per kilogram per minute, 4.85 c. c.

RESPIRATION EXPERIMENT No. C 20.

Date, October 26, 1909. Naked body-weight, 54.9 kilograms.

This experiment preceded the metabolism experiment of the same date and included four periods of the usual length and with the usual intermission. The soreness in the left nostril continued in this experiment. In the first period the adhesive plaster used about the mouth appeared to trouble the subject and he attempted to adjust it frequently. The pulse was also very weak in this period and it was difficult to count it accurately. The subject was very quiet in the

second period. The nosepieces were removed and reinserted between the third and fourth periods, but the adhesive plaster was not changed in any way. In the fourth period there was more or less activity of the upper part of the body. The subject moved his head once or twice as if the nosepieces troubled him. He tried to adjust the pillow and indicated that he thought the closure of the right nostril was not perfect, but on examination it was apparently all right. The results of the experiments are given in table 82.

TABLE 82.—*Results of respiration experiment No. C 20.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
October 26, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
8h 08m a.m.	9	58	177	238	0.74	63	14
8 27 a.m.	15	2	160	229	.70	67	14
8 52 a.m.	15	4	160	222	.72	66	14
9 15 a.m.	15	3	171	250	.68	71	14
Average			[1]167	[1]235	0.71	67	14

[1] Carbon dioxide eliminated per kilogram per minute, 3.04 c. c.; oxygen absorbed per kilogram per minute, 4.28 c. c.

RESPIRATION EXPERIMENT No. C 21.

Date, October 27, 1909. Naked body-weight, 54.9 kilograms.

This experiment included three periods, the two first 15 minutes in length and the last about 11 minutes, with the usual intermissions. In beginning the experiment some difficulty was experienced with the nosepieces, but another set was substituted, which proved satisfactory. The nosepiece was taken out of the left nostril and replaced between the second and third periods, but otherwise the conditions were unchanged throughout all the periods. The results may be found in table 83.

TABLE 83.—*Results of respiration experiment No. C 21.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
October 27, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
8h 25m a.m.	14	55	178	248	0.72	82	16
8 51 a.m.	14	51	174	251	.69	83	16
9 13 a.m.	11	23	175	245	.72	84	16
Average			[1]176	[1]248	0.71	83	16

[1] Carbon dioxide eliminated per kilogram per minute, 3.21 c. c.; oxygen absorbed per kilogram per minute, 4.52 c. c.

RESPIRATION EXPERIMENT NO. C 22.

Date, October 28, 1909. Naked body-weight, 56.1 kilograms.

This experiment included five periods, the first 10 minutes in length and the others 15 minutes long, with the exception of the last period, which was but 11 minutes. Previous to the experiment the subject lay on the couch for 20 minutes. The mouth was then closed with the adhesive plaster and the nosepieces carefully inserted and inflated. The soreness in the left nostril still troubled the subject, and to relieve him the nosepiece on the left side was released and reinflated between the second and third periods. Between periods three and four the subject rose and urinated. He talked considerably during this intermission and seemed in very good spirits. Both nosepieces were released and inserted again before the fourth period. The last period was not of full length, as the patient was feeling hungry. The results of this experiment are given in table 84.

TABLE 84.—*Results of respiration experiment No. C 22.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
October 28, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
8h 17m a.m.	10	0	157	241	0.65	59	14
8 34 a.m.	14	56	161	244	.66	58	14
8 56 a.m.	14	50	169	242	.70	67	14
9 31 a.m.	14	51	171	267	.64	66	13
9 53 a.m.	10	50	161	252	.64	70	14
Average			[1]164	[1]249	0.66	64	14

[1] Carbon dioxide eliminated per kilogram per minute, 2.92 c. c.; oxygen absorbed per kilogram per minute, 4.44 c. c.

RESPIRATION EXPERIMENT NO. C 23.

Date, October 29, 1909. Naked body-weight, 56.1 kilograms.

This experiment preceded the metabolism experiment which was made with the same subject on this date. Previous to the respiration experiment, the subject lay on the couch for 10 minutes, then the nosepieces and adhesive plaster were adjusted as in previous experiments. There were four separate periods of the usual length and with the usual intermissions. In the first period the plaster became loosened, but as the subject had had a great deal of experience with the apparatus and had been well trained in the routine, there is no reason to believe that he breathed through the mouth. At the end of the second period the nosepieces were released and reinserted before the next period, and they were removed again at the end of the third period. The pulse-rate rose considerably during the experiment, ranging from 50 to 60. This may have been due to the fact that the flies were very troublesome. The results are given in table 85.

TABLE 85.—*Results of respiration experiment No. C 23.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
October 29, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
$8^h 36^m$ a.m.	10	0	159	233	0.68	51	13
8 52 a.m.	14	0	158	234	.67	54	14
9 15 a.m.	14	53	162	236	.69	59	13
9 38 a.m.	15	0	158	235	.67	57	14
Average			[1]159	[1]235	0.68	55	14

[1] Carbon dioxide eliminated per kilogram per minute, 2.83 c. c.; oxygen absorbed per kilogram per minute, 4.19 c. c.

RESPIRATION EXPERIMENT No. C 24.

Date, October 30, 1909. Naked body-weight, 56.1 kilograms.

This experiment included five periods of the usual length. The subject lay on the couch about 15 minutes before the experiment began, then the nosepieces were inserted and the adhesive plaster adjusted. In the first period the plaster did not adhere perfectly, and the respirations did not seem the same as usual. The nosepieces were not removed between the first and second periods. At the end of the second period the subject cleared his throat, but was very sure that he lost no air through the mouth. Between the second and third periods the nosepieces were removed and reinserted. The subject was asked to move around considerably previous to the fourth period, and to keep moving during the experimental period. He accordingly moved his legs constantly and also moved his hands and arms considerably while reading his newspaper. The muscular activity was continued in the fifth period, although it was possibly somewhat less during this period than in the one preceding. The results of the experiment are given in table 86.

TABLE 86.—*Results of respiration experiment No. C 24.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
October 30, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
$8^h 21^m$ a.m.	9	52	164	230	0.71	50	13
8 40 a.m.	15	11	164	233	.70	52	13
9 07 a.m.	14	57	151	220	.68	53	13
Average			[1]160	[1]228	.70	52	13
$9^h 31^m$ a.m.	14	59	181	252	.72	59	14
9 54 a.m.	15	6	175	253	.69	56	13
Average			[1]167	[1]238	0.71	58	14

[1] Carbon dioxide eliminated per kilogram per minute, 2.85 c. c.; oxygen absorbed per kilogram per minute, 4.06 c. c. Periods beginning at $9^h 31^m$ a. m. and $9^h 54^m$ a. m. are excepted because of activity.

7

RESPIRATION EXPERIMENT No. C 25.

Date, October 31, 1909. Naked body-weight, 56.1 kilograms.

This experiment included five periods of the usual length. These were without incident the only difference being that in the last period the subject was muscularly active, considerably more so than during the two last periods in the previous experiment. The results of the experiment are given in table 87.

TABLE 87.—*Results of respiration experiment No. C 25.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
October 31, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
7h 56m a.m.	10	0	175	242	0.72	54	14
8 14 a.m.	14	55	164	238	.69	54	14
8 49 a.m.	15	1	156	230	.68	55	14
9 12 a.m.	14	55	148	220	.68	52	13
Average			[1]161	[1]232	0.69	54	14
9h 36m a.m.	14	57	[1]183	[1]249	0.73	66	13

[1] Carbon dioxide eliminated per kilogram per minute, 2.87 c. c.; oxygen absorbed per kilogram per minute, 4.14 c. c. Period beginning at 9h 36m a. m. is excepted because of activity.

GROUP I. CASE D.

DESCRIPTION OF THE CASE.

Male; 31 years of age; married; banker; came under observation December 27, 1909, 9 months after the onset of the disease.

Family history.—No family history of diabetes; father well at 70; mother died at 65 of "weak heart and grip"; one brother and one sister well. No children.

Personal history.—Chronic diarrhœa in 1897 lasting for 3 years. In 1905, renal calculus. In 1897, lost sight of one eye by accident.

Present illness.—Since March, 1909, blurring eyesight, polyuria (3 quarts in one night), polydipsia, but appetite not abnormal. Weariness. Riggs' disease. During October and November ate considerable sugar, although very little formerly. The disease was not diagnosed until September, 1909. Tobacco, excessive. Greatest weight, 57.3 kilograms, in 1900; average weight, 51.8 to 54.5 kilograms; August 30, 1909, 51.8 kilograms; September 28, 1909, 47 kilograms; December 27, 1909, 45.9 kilograms.

Physical examination.—Weak, pale, thin. Pupils unequal but react; pulse, 80, regular; tongue coated, moist; knee jerks normal; no edema, and nothing abnormal found in heart, lungs, or abdomen.

General treatment and history of case.—Treatment of this case did not begin until 6 months after the onset of the disease. This may account in part for the

poor condition of the patient when he was first observed. Added to this was the fact that he ate an unusual quantity of sugar a short time before coming under treatment. The patient was at the New England Deaconess Hospital from the latter part of September until the latter part of October. During this time he gained a little in strength, but the increase in weight was slight. On no occasion did he appear to overcome the debility which was present when he first came under observation. The history of the case is shown by the chart herewith (table 88).

The volume of urine was never excessive while under treatment, even when large quantities of sodium bicarbonate were administered. Albumen was either absent from the urine or present to only a very slight degree.

Acidosis.—The urine was acid at first, but became alkaline when 30 grams of sodium bicarbonate had been given daily for 3 days, followed by 3 days on which 45 grams daily were given. With a single exception it remained alkaline until October 24, although the quantity of sodium bicarbonate was decreased to 2 grams. The alkali was then omitted.

Diacetic acid.—This was strongly positive at the start, but gradually decreased with the administration of sodium bicarbonate, and altogether disappeared about 2 weeks after treatment began. It reappeared 2 months before death.

The quantity of sugar in the urine was never excessive while the patient was under observation, and there was soon acquired a slight positive carbohydrate-balance. This disappeared after some 3 weeks, and was never regained, except upon November 3, when 200 grams of carbohydrates were given in the form of oatmeal. The carbohydrate-balance upon this day was 120 grams, but upon the following day, the minus carbohydrate-balance was distinctly greater than it had previously been for some time, and the same holds true of the next day. During the latter part of the patient's life he was away from observation, and consequently it is not possible to give his exact diet, or to record the exact quantity of alkali which he was taking. Presumably the diet contained somewhat more than 50 grams of carbohydrates and the alkali amounted to about 20 grams of sodium bicarbonate each day. Toward the end he failed quite rapidly, and died in coma January 13, 1910.

EXPERIMENTS WITH CASE D.

This subject was in a hospital on a hospital régime. No calorimeter experiments were made with him and only three respiration experiments. The vital statistics were as follows:

Date of birth, 1878; range of naked body-weight, 48 to 50 kilograms.

RESPIRATION EXPERIMENT NO. D 1.

Date, October 1, 1909. Naked body-weight, 48 kilograms.

The subject came to the laboratory in the morning at $8^h 08^m$ a. m., without having had food, and lay down on the couch 20 minutes before the experiment

TABLE 88.—*Clinical chart—Case D.*

Date.	Experiment No.	Volume of urine.	Specific gravity.	Reaction.	Diacetic acid.	Nitrogen.	Sugar.			Diet.		Carbohydrate-balance.	$NaHCO_3$.	Naked body-weight.
							By Citron.	Fermentation.	By rotation.	Carbohydrate.	Alcohol.			
1909.		*c. c.*				*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*
Sept. 27–28	......	....	1037	ac.	+ + + +	..	..	..	[1] 5.2	..	..	..	..	47·0
Sept. 28–29	......	1890	1033	ac.	+ + +	..	..	..	76	75	..	0	30	47·0
Sept. 29–30	......	2670	1030	ac.	+ + + +	..	..	..	91	75	..	− 15	30	47·3
Sept. 30–Oct. 1	......	2100	1033	ac.	....	..	..	..	76	75	6	0	30	47·9
Oct. 1–2	**D 1**	**1680**	**1030**	ac.	+ + + +	..	..	..	**37**	**55**	**12**	**−20**	**45**	**48.9**
Oct. 2– 3	......	2220	1030	Sl.alk.	+ + + +	..	..	..	58	60	12	0	45	49.1
Oct. 3– 4	......	2310	1032	alk.	+ + + +	..	111	..	..	60	12	− 50	45	49.5
Oct. 4– 5	......	2760	1026	alk.	+ +	..	49	..	..	55	18	+ 5	41	49.9
Oct. 5–6	**D 2**	**2310**	**1025**	alk.	+ +	**13**	**42**	..	..	**45**	**18**	**+ 5**	**38**	**50.5**
Oct. 6– 7	......	2910	1026	alk.	+ +	..	38	..	..	45	18	+ 5	34	49.7
Oct. 7– 8	......	2550	1022	alk.	+ +	..	28	..	..	45	18	+ 15	34	49.6
Oct. 8– 9	......	1845	1015	alk.	+	..	6	..	..	[4] 30	6	+ 25	12	47.7
Oct. 9–10	......	1110	1013	alk.	+	..	0	..	..	45	6	+ 45	12	48.9
Oct. 10–11	......	2250	1021	alk.	+ +	..	..	..	27	45	6	+ 15	5.5	49.1
Oct. 11–12	......	2880	1014	alk.	0	..	..	..	23	45	6	+ 20	12	48.2
Oct. 12–13	......	2280	1018	alk.	0	..	..	..	23	45	6	+ 20	12	48.0
Oct. 13–14	......	2160	1020	alk.	0	..	..	..	17	[5] 10	6	− 5	10	48.2
Oct. 14–15	**D 3**	**2310**	**1014**	alk.	**0**	..	**0**	..	..	**15**	**6**	**+15**	**8**	**48.3**
Oct. 15–16	......	2640	1011	alk.	?	..	0	..	..	15	6	+ 15	6	48.4
Oct. 16–17	......	2700	1013	Sl.ac.	0	..	..	..	5	15	6	+ 10	6	47.8
Oct. 17–18	......	3030	1018	alk.	....	..	..	..	36	15	6	− 20	4	47.7
Oct. 18–19	......	2160	1024	alk.	0	..	..	..	35	13	6	− 22	4	48.1
Oct. 19–20	......	2370	1023	alk.	0	..	..	..	28	13	..	− 15	2	47.9
Oct. 20–21	......	2160	1024	Sl.alk.	0	..	..	..	30	13	..	− 17	2	47.9
Oct. 21–22	......	1980	1022	alk.	0	..	..	..	16	13	..	− 3	2	48.2
Oct. 22–23	......	1800	1022	....	0	..	..	..	18	..	..	..	..	48.4
Oct. 24–25	......	1800	1022	ac.	Sl. +	..	..	..	22	15	..	− 5	..	....
Oct. 25–26	......	1900	1025	ac.	0	..	..	..	34	15	..	− 20	..	....
Oct. 26–27	......	1750	1025	....	0	..	..	21	..	10	..	− 10	..	....
Oct. 27–28	......	2230	1023	....	0	..	..	19	..	10	..	− 10	..	....
Oct. 28–29	......	1850	1029	....	....	..	..	11	..	13	..	0	..	49.1
Oct. 29–30	......	1900	1025	....	....	..	..	16	..	13	..	− 5	..	....
Oct. 30–31	......	1850	1022	....	....	..	..	15	..	10	..	− 5	..	....
Oct. 31–Nov. 1	......	2000	....	....	....	..	..	16	..	10	..	− 5	..	....
Nov. 1– 2	......	1780	....	....	....	..	..	11	..	13	..	0	..	....
Nov. 3– 4	......	3000	1022	....	....	..	..	81	..	[6] 200	..	+120	..	....
Nov. 4– 5	......	1900	1025	....	....	..	..	48	..	10	..	− 40	..	....
Nov. 5– 6	......	1800	1025	....	....	..	..	47	..	10	..	− 35	..	....
Nov. 6– 7	......	1400	1028	....	....	..	..	42	..	..	..	..	..	....
Nov. 8– 9	......	2000	1022	....	+	..	..	22	..	..	..	..	..	....
Nov. 9–10	......	1720	1024	....	+	..	..	19	..	..	..	..	..	....
Nov. 10–11	......	1420	1021	....	+	..	..	9	..	..	..	..	.	....
Nov. 11–12	......	1900	1025	....	+	..	..	8	..	..	..	..	20	....
Nov. 12–13	......	1000	1026	....	+	..	..	2	..	..	..	..	0	....
Nov. 13–14	......	1250	1026	....	+	..	..	10	..	..	..	..	0	51.1
Nov. 14–15	......	1900	1018	....	+	..	..	11	..	..	..	..	0	....
Nov. 15–16	......	2000	1016	....	+ +	..	..	4	..	..	..	..	0	....
Nov. 16–17	......	1800	1017	....	+ +	..	..	7	..	..	..	..	.0	49.8
Nov. 21–22	......	1706	1026	....	Sl. +	..	..	..	34	25	..	..	..	....
Nov. 22–23	......	1450	1020	....	+ +	..	..	7	..	..	..	..	0	49.9
Nov. 28–29	......	1900	1022	....	+ +	..	..	11	..	..	..	..	0	50.9
Dec. 5– 6	......	1760	1022	....	+	..	..	18	..	50	..	..	20±	51.0
Dec. 13–14	......	1750	1024	....	+	..	..	14	..	50	..	..	20±	....
Dec. 20–21	......	2000	1025	....	+ +	..	..	16	..	50	..	..	20±	....
1910.														
Jan. 2– 3[2]	......	1875	1023	....	+ +	..	..	13	..	50	..	..	20±	48.1
Jan. 10–11[3]	......	2000	1024	....	+ +	..	..	14	..	50	..	..	20±	....
Jan. 13	Died.													

[1] Per cent.
[2] Loss of energy. Exercising much. Dieting strictly.
[3] Colds. Inflamed tooth, much pain, weak.
[4] Oatmeal and starvation.
[5] Vegetable day.
[6] Oatmeal day.

proper began. This experiment was divided into four periods, the first of 10 minutes, and the other three of 15 minutes each, with the usual intermissions. The subject rose from the couch and passed urine at the end of the second period, and again at the end of the last period. The results of the experiment are given in table 89, and the statistics of urine in table 90.

TABLE 89.—*Results of respiration experiment No. D 1.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
October 1, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
$8^h 07^m$ a.m.	10	3	163	215	0.75	53	16
8 33 a.m.	15	..	155	221	.70	55	17
8 59 a.m.	15	1	153	212	.72	55	18
9 23 a.m.	15	3	154	204	.75	56	17
Average			[1]156	[1]213	0.73	55	17

[1] Carbon dioxide eliminated per kilogram per minute, 3.25 c. c.; oxygen absorbed per kilogram per minute, 4.44 c. c.

TABLE 90.—*Statistics of urine—Respiration experiment No. D 1.*

Date and period.	Volume.	Total nitrogen.	Sugar.	D : N.
October 1, 1909.	*c. c.*	*grams.*	*grams.*	
$7^h 00^m$ a.m. to $8^h 47^m$ a.m.	118	1.06	3.4	3.21
8 47 a.m. 9 44 a.m.	52	.42	1.2	2.86

The large excretion of carbon dioxide frequently noticed in experiments of this kind is here present. The last three experiments show a wonderfully constant carbon-dioxide excretion per minute with this subject. The oxygen consumption varies somewhat but not beyond usual limits, and the respiratory quotient ranges from 0.7 to 0.75, the average for the four periods being 0.73. The pulse-rate and respiration-rate did not undergo material changes throughout the whole experiment.

The subject was an unusually good one in that he cooperated to the fullest degree with the experiment and remained perfectly quiet on the couch, with a very regular respiration-rate. He was not annoyed or prejudiced at all by the experimentation.

RESPIRATION EXPERIMENT No. D 2.

Date, October 5, 1909. Naked body-weight, 50 kilograms.

This experiment was divided into four separate periods of the usual lengths and intermissions. The subject came to the laboratory without breakfast and lay on the couch for 20 minutes before the experiment began. The nosepieces were then adjusted and an attempt made to use the adhesive plaster. On account

of the subject's beard the plaster did not adhere, and it was removed before the beginning of the second period, as it seemed to be of no use. The subject remained lying on the couch throughout the four periods. Between the second and third period, the nosepieces were released and readjusted, and in the third period the subject indicated that there was a leak in the left nosepiece. This nosepiece was then tightened without loss of pressure. At the beginning of the fourth period the subject said there was moisture in the nosepieces and another set was substituted. Unfortunately, in the last two periods the determination of the oxygen consumption was lost. The results of the experiment are given in table 91.

TABLE 91.—*Results of respiration experiment No. D 2.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
October 5, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
8h 20m a.m.	10	40	152	208	0.73	53	16
8 39 a.m.	15	3	153	205	.75	54	17
9 04 a.m.	14	47	153	...	....	55	17
9 36 a.m.	14	43	159	...	....	57	17
Average			[1]154	[1]207	0.74	55	17

[1] Carbon dioxide eliminated per kilogram per minute, 3.08 c. c.; oxygen absorbed per kilogram per minute, 4.14 c. c. The urine collected between 7 a. m. and 9h 55m a. m. amounted to 143 c. c. and contained 1.73 grams of nitrogen and 2.9 grams sugar, giving a D : N ratio of 1.68.

As may be seen, the carbon-dioxide production was remarkably constant, and in the two periods in which the oxygen was determined the same amount was found in each case. The pulse-rate slightly increased in the fourth period. In this experiment, as in the preceding one, the subject was very quiet and cooperated in every way towards the success of the experiment.

RESPIRATION EXPERIMENT No. D 3.

Date, October 14, 1909. Naked body-weight, 48.3 kilograms.

The subject came to the laboratory without breakfast, as in the preceding experiments, and lay on the couch for about 10 minutes before the experiment began. The nosepieces were then adjusted, and although the adhesive plaster was used it was not very effective, owing to the stiff mustache of the subject. During the third period the subject swallowed, but as he did not open his mouth, it is not probable that any air was lost. At the end of the experiment he complained that lying still so long made his neck ache. Immediately after the experiment he passed 223 c. c. of urine and returned to the hospital. The results of the metabolism are given in table 92.

The results for both carbon dioxide and oxygen are certainly as good as can be expected in physiological experimentation, and evidently these values may

be taken as signifying the respiratory exchange for this subject under the conditions then existing. The relatively high respiratory quotient in this experiment signifies that the subject had no inconsiderable storage of glycogen which he could draw upon when food was not ingested. An examination of the urine chart will prove of unusual interest. It is rather difficult to understand why this subject, with such a relatively high respiratory quotient, should have died shortly afterwards in coma; the only explanation apparent at present is that the diet was so rigidly restricted that the store of glycogen was drawn upon to such an extent as to induce acidosis.

TABLE 92.—*Results of respiration experiment No. D 3.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
October 14, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
$8^h 30^m$ a.m.	10	3	147	190	0.77	53	16
8 46 a.m.	14	57	144	194	.74	57	16
9 13 a.m.	15	34	145	192	.76	56	16
9 34 a.m.	14	57	142	197	.72	55	17
Average			[1]145	[1]193	0.75	55	16

[1] Carbon dioxide eliminated per kilogram per minute, 3.00 c. c.; oxygen absorbed per kilogram per minute, 4.00 c. c. The urine collected from 7 a. m. to $9^h 50^m$ a. m. amounted to 223 c. c. and contained 1.21 grams of nitrogen and 0.6 gram of sugar, giving a D : N ratio of 0.50.

GROUP I. CASE E.

Male; born, 1890; single; light farm work; came under observation November 9, 1908.

Family history.—No family history of diabetes. Father, mother, and one sister well.

Past history.—Good health up to onset of diabetes.

Present illness.—First symptom of diabetes occurred in September, 1907. Polyphagia and polydipsia were extreme. No loss of strength.

Physical examination.—Height, 173 centimeters. Weight, February, 1908, 67.2 kilograms, dressed. Well developed and nourished, good color, skin dry, good teeth, pupils equal and react to light, knee jerks normal. Examination of heart, lungs, and liver negative. Pulse regular, and of good volume and tension.

General treatment and history of case.—The patient entered the New England Deaconess Hospital November 9, 1908, and remained in the hospital until November 18. His condition continued to be fairly good and he maintained a weight of about 66.2 kilograms. He was able to do light work. The prescribed diet was followed to a moderate degree. In September, 1909, he was much troubled with indigestion, and although his weight was not affected he steadily lost ground and died of coma on October 13, 1909. The history of the case is shown by the chart herewith (table 93).

TABLE 93.—*Clinical chart—Case E.*

Date.	Experiment No.	Volume of urine.	Specific gravity.	Diacetic acid.	β-oxybutyric acid.	Nitrogen.	Ammonia. Total.	Ammonia. $\frac{NH_3-N}{Total\ N}$	Sugar. By Citron.	Sugar. Fermentation.	Sugar. By rotation.	Diet. Carbohydrate.	Diet. Protein.	Diet. Nitrogen.	Diet. Fat.	Diet. Alcohol.	Diet. Calories.	Carbohydrate-balance.	$NaHCO_3$.	Naked body-weight.
1908.		*c. c.*			*gms.*	*gms.*	*gms.*	*p. ct.*	*gms.*	*p. ct.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*		*gms.*	*gms.*	*kilos.*
Feb. 25–26	....	....	1034	....	....	....	..	....	+[3]	..	..	..	..	..	...	..	....	..	..	....
Mar. 1–2	....	....	1024	....	....	....	..	....	+[3]	..	..	..	..	..	...	..	....	..	..	....
Apr. 10–11	....	....	1026	0	....	....	..	....	+[3]	..	..	..	..	..	...	..	....	..	..	....
May 19–20	....	....	1029	0	....	....	..	....	+[3]	..	..	..	..	..	...	..	....	..	..	....
June 18–19	....	....	1026	0	....	....	..	....	+[3]	..	..	..	..	..	...	..	....	..	..	....
July 13–14	....	....	1031	0	....	....	..	....	+[3]	..	..	..	..	..	...	..	....	..	..	....
Aug. 14–15	....	....	1025	0	....	....	..	....	+[3]	..	..	..	..	..	...	..	....	..	..	....
Oct. 1–2	....	....	1031	0	....	....	..	....	....	..	..	..	..	..	...	..	....	..	..	....
Oct. 13–14	....	....	1031	(?)	....	....	..	....	....	4.2	..	..	..	..	...	..	....	..	..	....
Nov. 2–3	....	2000	1028	+	....	5.72	..	....	....	5.1	88	..	..	..	...	..	....	..	..	....
Nov. 3–4	....	1750	1030	+	....	....	..	....	....	..	84	..	..	..	...	..	....	..	..	....
Nov. 4–5	....	2050	1033	+	....	....	..	....	....	..	118	..	..	..	...	..	....	..	..	....
Nov. 5–6	....	1950	1035	+	....	10.13	..	....	118	..	103	..	..	..	...	..	....	..	..	....
Nov. 6–7	....	1740	1033	Sl. +	....	6.35	1.1	14.3	120	..	104	..	..	..	...	..	....	..	..	....
Nov. 7–8	....	1400	1037	+ +	....	9.18	2.0	17.9	83	..	72	..	..	..	...	..	....	..	..	....
Nov. 8–9	....	1250	....	....	....	9.8	2.1	17.6	78	..	..	..	..	..	...	..	....	..	..	....
Nov. 9–10	**E 1**	**1710**	....	....	**17.9**	**12.5**	**3.1**	**20.4**	**75**	..	**63**	..	..	..	...	..	....	..	..	....
Nov. 10–11	**E 3**	**2230**	....	....	**13.5**	**16.0**	**3.8**	**19.6**	**91**	..	..	..	..	..	...	..	....	..	..	....
Nov. 11–12	....	1520	....	....	....	14.6	..	....	71	..	67	20	88	14	...	0	....	..	8	58.6
Nov. 12–13[1]	....	2070	....	....	....	8.2	..	....	129	..	124	30	113	18	220	0	2600	−100	8	58.6
Nov. 13–14[1]	....	1175	1036	+	....	5.4	..	....	74	..	71	30	113	18	220	0	2600	− 45	8	59.0
Nov. 14–15[1]	....	1125	1037	+ +	....	7.9	..	....	63	..	65	30	113	18	220	0	2600	− 35	8	58.7
Nov. 15–16[2]	....	1600	1035	+ +	....	10.4	..	....	87	..	80	60	116	18.5	220	0	2700	− 25	8	58.8
Nov. 16–17	**E 2**	**1805**	....	....	**11**	**14.4**	**3.3**	**18.9**	**82**	..	**76**	**36**	**78**	**12.5**	**145**	**12**	**1800**	**−45**	**4**	**59.3**
Nov. 17–18	**E 4**	**1955**	....	....	**12.1**	**18.5**	**3.3**	**14.7**	**98**	..	**89**	..	..	..	...	..	....	..	..	....
Dec. 28–29	....	....	1032	0	....	....	..	....	....	5.5	..	..	..	..	...	..	....	..	..	....
1909.																				
Jan. 5–6	....	....	1032	(?)	....	....	..	....	....	4.6	..	..	..	..	...	..	....	..	..	....
Jan. 13–14	....	....	1028	0	....	....	..	....	....	4.4	..	..	..	..	...	..	....	..	..	....
Jan. 29–30	....	....	1030	+ +	....	....	..	....	....	4.6	..	..	..	..	...	..	....	..	..	....
Feb. 12–13	....	....	1036	0	....	....	..	....	....	6.0	..	..	..	..	...	..	....	..	..	....
Feb. 26–27	....	....	1030	+	....	....	..	....	+	..	..	..	..	..	...	..	....	..	..	....
Mar. 12–13	....	....	1034	+ +	....	....	..	....	....	4.6	..	..	..	..	...	..	....	..	..	....
Mar. 28–29	....	....	1030	+	....	....	..	....	....	4.1	..	..	..	..	...	..	....	..	..	....
Apr. 11–12	....	....	1030	+ +	....	....	..	....	....	4.6	..	..	..	..	...	..	....	..	..	....
Apr. 30–May 1	....	....	1028	+	....	....	..	....	....	5.1	..	..	..	..	...	..	....	..	..	....
May 21–22	....	....	1028	+	....	....	..	....	....	4.8	..	..	..	..	...	..	....	..	..	....
Oct. 13	Died.																			

[1] 4 eggs, 240 g. meat, 240 c. c. cream, 300 g. vegetables, 18 g. oatmeal, 15 g. oil, 90 g. cheese, 120 g. butter.

[2] The same as on November 12-13, and 50 g. bread.

[3] Fehling's test.

The records of the volumes of urine are incomplete prior to and succeeding the stay of the patient at the hospital. While there the quantity was nearly normal. The reaction was acid. Albumen was absent throughout or present to only an extremely slight degree. Diacetic acid first appeared upon November 3, 1908, and increased in intensity. β-oxybutyric acid was present to a considerable degree in November, 1908, varying from 11 grams to 17.9 grams per day. Ammonia in November, 1908, was considerable, rising to 3.8 grams per day, the $NH_3-N:N$ exceeding 20 per cent. The acidosis is also shown by the difference between the amount of sugar obtained by the polariscope and by the Citron test.

The quantity of sugar did not exceed 129 grams per day while the patient was in the hospital, but this was evidently below the previous amounts present because the carbohydrate-balance fell from —120 grams on the 12th–13th to —35 grams 2 days subsequently. The patient during his stay at the hospital did not bear the diet comfortably, and suspicion was awakened that errors might have entered into either the quantities of urine or diet which he reported outside of the hospital.

EXPERIMENTS WITH CASE E.

There were four metabolism experiments carried out with this subject, two after a 12-hours' fast, and without breakfast, and two preceded by food. No respiration experiments were made with him. The vital statistics were as follows:

Date of birth, 1890; height, 173 centimeters; body-weight, 60 kilograms.

METABOLISM EXPERIMENT NO. E 1.

Date, November 9, 1908. Naked body-weight, 60 kilograms.

This experiment was carried out after a 12-hours' fast, the subject coming to the laboratory without breakfast. He entered the chamber of the chair calorimeter at $8^h\ 05^m$ a. m. and the experiment began at $9^h\ 02^m$ a. m. The measurements of the metabolism were made in three 2-hour periods, and the experiment ended at $3^h\ 02^m$ p. m. The water taken by the subject was as follows: $9^h\ 02^m$ a. m., 6 c. c.; $11^h\ 02^m$ a. m., 13 c. c.; $1^h\ 02^m$ p. m., 15 c. c. The subject was weighed at the end of each period, and he also telephoned several times. About the middle of the first period it was found that he was playing cards and he was asked not to continue this. After the experiment he stated that he played only about 5 minutes. The subject said that the time seemed to pass rapidly, although he asked over the telephone several times how much longer the experiment would continue.

The pulse-rate was counted by the subject himself, but the noise of the blower used in the ventilating current interfered somewhat in his taking the record, especially in the first part of the experiment, and he did not consider the records reliable. The record throughout the experiment was 77. The measurements of the body-temperature were made sublingually by the subject. The measurements of the metabolism are given in table 94, and the statistics of urine in table 97.

TABLE 94.—*Measurements of metabolism—Metabolism experiment No. E 1.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.[1]
November 9, 1908.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
$9^h 02^m$ a.m. to $11^h 02^m$ a.m. .	51.0	50.7	216	296	46.5	0.73	172	77
11 02 a.m. 1 02 p.m. .	47.5	49.3	202	288	59.1	.70	169	77
1 02 p.m. 3 02 p.m. .	45.9	46.3	195	270	43.7	.72	158	77
Total 6 hours[2]......	144.4	146.3	204	284	149.3	....	[3]499	..

[1] Pulse by the subject.
[2] Carbon dioxide eliminated per kilogram per minute, 3.40 c. c.; oxygen absorbed per kilogram per minute, 4.73 c. c.; heat eliminated per kilogram per hour, 1.38 calories.
[3] Sublingual body-temperature at beginning 37.22° C.; at end, 37.06° C. Heat production for total 6 hours 490 calories.

There was a slight decrease in metabolism as the experiment progressed, as would be expected, since this was the first experiment with the subject and the novelty did not wear off until the end of the experiment. The records of the observer show that the subject was more or less active in the early part of the experiment. While the pulse-rate records are exceedingly unreliable the value 77 probably represents the average for the total 6 hours.

METABOLISM EXPERIMENT No. E 2.

Date, November 16, 1908. Naked body-weight, 60 kilograms.

Like the preceding experiment, this was carried out after a 12-hours' fast, the subject coming to the laboratory without breakfast. He entered the chair calorimeter at $8^h 17^m$ a. m. and the experiment began at $9^h 21^m$ a. m., continuing for three 2-hour periods. The experiment ended at $3^h 21^m$ p. m. Water was taken as follows: $9^h 30^m$ a. m., 17 c. c.; $11^h 30^m$ a. m., 41 c. c.; $1^h 30^m$ p. m.,

TABLE 95.—*Measurements of metabolism—Metabolism experiment No. E 2.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen. absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.[1]
November 16, 1908.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
$9^h 21^m$ a.m. to $11^h 21^m$ a.m. .	41.4	49.5	176	289	46.4	0.61	157	80
11 21 a.m. 1 21 p.m. .	46.8	43.6	199	254	44.2	.78	157	79
1 21 p.m. 3 21 p.m. .	46.9	40.1	199	234	46.4	.85	156	80
Total 6 hours[2]......	135.1	133.2	191	259	137.0	....	[3]470	..

[1] Pulse by the subject.
[2] Carbon dioxide eliminated per kilogram per minute, 3.18 c. c.; oxygen absorbed per kilogram per minute, 4.32 c. c.; heat eliminated per kilogram per hour, 1.30 calories.
[3] Sublingual body-temperature at beginning, 37.11° C.; at end, 36.78° C. Heat production for total 6 hours, 453 calories.

37 c. c.; and at $2^h 45^m$ p. m., 51 c. c. The subject stated that he was very much more tired after this experiment than after the previous one.

The pulse-rate records were made by the subject himself and ranged from 77 to 83. The body-temperature measurements were made sublingually by the subject with a clinical thermometer for the beginning of each period and at the end of the experiment. The measurements of the metabolism are given in table 95. The statistics of the urine are given in table 99.

The results indicate a marked increase in the carbon-dioxide excretion in the second and third period, with a corresponding decrease in the oxygen absorption. On the other hand, the heat-elimination was remarkably constant for all three periods.

Metabolism Experiment No. E 3.

Date, November 10, 1908. Naked body-weight, 60 kilograms.

This experiment differed from those preceding in that the subject ingested food immediately after entering the calorimeter chamber the purpose being to test the effect on the metabolism of the ingestion of a large amount of protein. He therefore came to the laboratory without breakfast and entered the calorimeter chamber at $7^h 52^m$ a. m., then ate 329 grams of broiled beefsteak, finishing at $8^h 20^m$ a. m. The experiment began at $8^h 54^m$ a. m. and continued for three 2-hour periods, ending at $2^h 54^m$ p. m. The amounts of water consumed during the experiment were as follows: $8^h 59^m$ a. m., 60 c. c.; $12^h 59^m$ p. m., 66 c. c.; $2^h 30^m$ p. m., 65 c. c. The subject sat in a swinging chair throughout the whole experiment and was weighed in it at the end of every period. During one of the weighings he dropped a pencil, which caused more activity than usual. At 1 p. m. the subject stated that he felt better than he had in previous experiments. Later he also said that the time had passed rapidly, that the beefsteak, which he brought with him to the laboratory, tasted good, and he could have eaten more if it had not been dry. The footrest broke during the second period, and as his feet did not touch the floor it gave him some discomfort and caused more restlessness. He telephoned several times during the experiment.

The pulse-rate was counted by the subject, but inasmuch as the rate for the whole experiment was 77, it is doubtful if this can be relied upon. After he left the calorimeter it was counted by one of the assistants, the first count being 100, and the second taken almost immediately, 90, and a subsequent count was 80. The body-temperature measurements were taken as usual sublingually by the subject for the beginning of each period and at the end of the experiment. The measurements of the metabolism are given in table 96, and the statistics of urine in table 97.

There was a noticeable increase in the carbon-dioxide elimination and oxygen consumption in the last period. The heat eliminated remained essentially the same throughout the whole experiment. The abnormally large water vaporization in the second period was doubtless due to a defective regulation of the temperature of the air in the calorimeter which caused a condensation of water and

a subsequent evaporation. Since this was one of the earlier experiments with this apparatus the technique had not been fully perfected, and consequently such irregularities would naturally be expected.

TABLE 96.—*Measurements of metabolism—Metabolism experiment No. E 3.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.[1]
			Carbon dioxide eliminated.	Oxygen absorbed.				
November 10, 1908.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
$8^h 54^m$ a.m. to $10^h 54^m$ a.m. .	53.7	57.2	228	334	41.9	0.68	191	77
10 54 a.m 12 54 p.m. .	54.2	57.5	230	335	67.2	.69	186	77
12 54 p.m. 2 54 p.m. .	58.3	59.1	247	345	45.6	.72	191	77
Total 6 hours[2]	166.2	173.8	235	338	154.7	. . . .	[3]568	. .

[1] Pulse by the subject.
[2] Carbon dioxide eliminated per kilogram per minute, 3.92 c. c.; oxygen absorbed per kilogram per minute, 5.63 c. c.; heat eliminated per kilogram per hour, 1.58 calories.
[3] Sublingual body-temperature at beginning, 37.00° C.; at end, 36.78° C. Heat production for total 6 hours, 556 calories.

TABLE 97.—*Statistics of urine—Metabolism experiments Nos. E 1 and E 3.*

Date and period.	Quantity.	Total nitrogen.	Sugar.		D : N.
			Polarization.	Titration.	
November 9–10, 1908.	*grams.*	*grams.*	*grams.*	*grams.*	
$7^h 00^m$ a.m. to $9^h 02^m$ a.m.	241	1.87	10.1	11.5	6.15
9 02 a.m. 11 02 a.m.	137	1.25	5.5	6.0	4.80
11 02 a.m. 1 02 p.m.	92	1.00	2.7	3.8	3.80
1 02 p.m. 3 02 p.m.	63	2.90	1.5	2.2	2.44
3 02 p.m. 8 00 a.m.	1170 c. c.	7.53	43.3	51.9	. . . .
November 10–11, 1908.					
$8^h 00^m$ a.m. to $8^h 54^m$ a.m.	215	1.03	. . . .	8.5	. . . .
8 54 a.m. 10 54 a.m.	219	1.07	. . . .	7.4	. . . .
10 54 a.m. 12 54 p.m.	269	2.12	. . . .	10.0	. . . .
12 54 p.m. 2 54 p.m.	168	2.14	. . . .	7.0	. . . .
2 54 p.m. 7 00 a.m.	1360 c. c.	9.61	. . . .	57.8	. . . .

METABOLISM EXPERIMENT NO. E 4.

Date, November 17, 1908. Naked body-weight, 60 kilograms.

This experiment was also designed to study the effect of the ingestion of protein. The subject came to the laboratory without breakfast and entered the chair calorimeter at 8 a. m. A considerable amount of beefsteak was broiled for him at the laboratory until well done, and of this he ate 402 grams between $8^h 25^m$ a. m. and $8^h 48^m$ a. m. The experiment began at $9^h 26^m$ a. m. and continued for three 2-hour periods, ending at $3^h 26^m$ p. m. Water was taken as follows: $8^h 45^m$ a. m., 73 c. c.; $12^h 30^m$ p. m., 71 c. c.; $1^h 30^m$ p. m., 99 c. c. The

subject was fairly quiet during the experiment, aside from the activity incidental to urinating, drinking water, and telephoning. After the experiment he stated that his head ached the last 2 hours, that his back became tired, and that he was uncomfortable inside the chamber, but after leaving the chamber he was more comfortable and felt better. He also said that he had no difficulty in eating all the meat that was given him.

The pulse-rate was taken as usual by the subject and ranged from 73 to 86. The measurements of body-temperature were made by the subject sublingually for the beginning of each period and at the end of the experiment. The results of the metabolism measurements are given in table 98. Statistics of urine are given in table 99.

TABLE 98.—*Measurements of metabolism—Metabolism experiment No. E 4.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.[1]
			Carbon dioxide eliminated.	Oxygen absorbed.				
November 17, 1908.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
$9^h 26^m$ a.m. to $11^h 26^m$ a.m..	52.0	53.9	221	315	60.0	0.70	171	83
11 26 a.m. 1 26 p.m..	52.0	53.5	221	312	58.4	.71	169	76
1 26 p.m. 3 26 p.m..	55.2	57.4	234	335	60.2	.70	171	80
Total 6 hours[2]......	159.2	164.8	225	321	178.6	....	[3]511	..

[1] Pulse by the subject.
[2] Carbon dioxide eliminated per kilogram per minute, 3.75 c. c.; oxygen absorbed per kilogram per minute, 5.35 c. c.; heat eliminated per kilogram per hour, 1.42 calories.
[3] Sublingual body-temperature at beginning, 37.06° C.; at end, 36.78° C. Heat production for total 6 hours, 496 calories.

TABLE 99.—*Statistics of urine—Metabolism experiments Nos. E 2 and E 4.*

Date and period.	Quantity.	Total nitrogen.	Sugar.		D : N.
			Polarization.	Titration	
November 16–17, 1908.	*grams.*	*grams.*	*grams.*	*grams.*	
$7^h 00^m$ a.m. to $9^h 21^m$ a.m.......	266	2.26	15.2	14.2	6.28
9 21 a.m. 11 21 a.m.......	153	1.49	7.0	7.3	4.90
11 21 a.m. 1 21 p.m.......	105	1.25	4.2	4.8	3.84
1 21 p.m. 3 21 p.m.......	161	.85	2.1	2.5	2.94
3 21 p.m. 7 00 a.m.......	1120 c. c.	8.54	47.0	52.7	....
November 17–18, 1908.					
$7^h 00^m$ a.m. to $8^h 07^m$ a.m.......	127	.92	7.1	7.2	....
8 07 a.m. 9 26 a.m.......	165	1.26	8.9	9.6	....
9 26 a.m. 11 26 a.m.......	275	2.26	14.3	14.4	....
11 26 a.m. 1 26 p.m.......	216	2.20	10.1	11.0	....
1 26 p.m. 3 26 p.m.......	165	2.47	7.9	8.5	....
3 26 p.m. 7 00 a.m.......	1005 c. c.	9.41	40.2	47.7	....

The metabolism was relatively constant for the three periods, there being a slight increase in both carbon dioxide and oxygen in the third period. The heat elimination was constant throughout the whole three periods; owing to the fact that there was a perceptible decrease in body-temperature of 0.5° in the 6 hours, the total heat-production for the experiment is lowered by some 15 calories. The uncertain values of the measurements of body-temperature obtained by the clinical thermometer make this value for heat-production somewhat speculative.

COMPARISON OF METABOLISM EXPERIMENTS WITH CASE E.

This subject did not appreciate the scientific aspects of the experiments in which he was to participate, consequently the results have not the significance of the results obtained with other subjects who cooperated with us more fully. A comparison of the results of the experiments is given in table 100.

TABLE 100.—*Comparison of metabolism experiments with Case E.*

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Respiratory quotient.	Heat eliminated per hour.	Heat produced per hour.	Average pulse per minute.
EXPERIMENTS WITHOUT FOOD.									
		kilos.	*hrs.*	*c. c.*	*c. c.*		*cals.*	*cals.*	
E 1	Nov. 9, 1908	60	6	204	284	0.72	83	82	77
E 2	Nov. 16, 1908	60	6	191	259	.74	78	75	80
EXPERIMENTS WITH FOOD.									
E 3	Nov. 10, 1908 [1]	60	6	235	338	0.70	95	93	77
E 4	Nov. 17, 1908 [2]	60	6	225	321	.70	85	83	80

[1] 34 minutes before the experiment began, the subject finished eating 329 grams of cooked beefsteak.
[2] 38 minutes before the experiment began, the subject finished eating 402 grams of cooked beefsteak.

The results of the two experiments without food show a fairly uniform agreement. Less carbon dioxide and less heat were eliminated, however, in the second experiment and less oxygen was consumed. This may be accounted for by the diminished muscular activity of the subject in the second experiment. The experiments with food show a noticeable increase in metabolism as measured by the carbon-dioxide elimination, oxygen consumption and heat-production. There was also a slight increase in the pulse-rate, although the records are open to criticism. The respiratory quotient was low in all the experiments.

GROUP I. CASE F.

DESCRIPTION OF THE CASE.

Male; born September 16, 1885; farmer; married; came under observation July 14, 1908.

Family history.—Father, mother, and two brothers well. No children. Married January 8, 1907. The wife's mother, second cousin, and great-aunt also had diabetes.

Past history.—St. Vitus' dance, otherwise unusually good health, except for infrequent attacks of indigestion and headache.

Present illness.—The onset was approximately 1 year after marriage, but it was not diagnosed until March, 1908. The greatest weight was 84.4 kilograms, and 58.1 kilograms was the lowest weight reached. Polyuria and cramps in the legs were the noticeable symptoms. The greatest quantity of urine noticed was 5000 c. c.

Physical examination.—A robust-looking young farmer, whose loss of weight was not striking. Height, 176 centimeters. Nothing abnormal was noted upon physical examination (original data not at hand).

General treatment and history of the case.—The patient remained at home in the White Mountains from the middle of July, 1908, until early in September, 1908. During this time the quantity of sugar did not noticeably decrease, but remained about 7 per cent, and the total quantity excreted each day varied from 103 grams to 230 grams upon August 14. The quantity of ammonia increased from 1.5 grams on July 13 to 4.2 grams on August 14. The patient entered the New England Deaconess Hospital September 13, 1908, and remained in the hospital until October 2. During this time the diet was gradually restricted, and the carbohydrates finally reduced to 10 grams daily, and a single vegetable day given. The quantity of sugar in the urine decreased noticeably, but only upon 2 days was the patient sugar-free. The carbohydrate-balance was generally minus, ranging from minus 60 grams to plus 10 grams. Upon leaving the hospital the sugar promptly increased, but during the next month did not rise, when examined, to above 65 grams. In the subsequent year, 1909, several analyses were made, and a progressive increase was noted. No analyses were recorded after May 3, 1909. The history of the case is shown in the chart herewith (table 101).

The urine remained acid, whenever it was examined, with the exception of 6 days at one period and 1 day at another. Upon these 6 days, and for the preceding 5 days, sodium bicarbonate was administered in considerable quantities; during the 5 days preceding the time the urine was alkaline, and the 6 consecutive days in which it had this reaction, in all 192 grams of sodium bicarbonate were given.

Diacetic acid was present whenever the test was applied, except on two occasions.

The quantity of β-oxybutyric acid during the first few weeks of observation

was rather low, being 7.1 grams on July 15, and 8.5 grams on September 1 to 2. It was not later examined.

The ammonia increased to 4.2 grams while the patient was in the hospital, but later diminished, as shown by a single analysis. Although the patient was not seen after October 2, 1908, he frequently reported himself as being in fair condition. He died of pneumonia in February, 1910, which involved the right lower lobe of the lung. Coma was not present. Had it not been for the pneumonia there was no especial indication that he would have so quickly succumbed to the disease.

TABLE 101.—*Clinical chart—Case F.*

Date.	Experiment No.	Volume of urine.	Specific gravity.	Reaction.	Diacetic acid.	β-oxybutyric acid.	Nitrogen.	Ammonia. Total.	Ammonia. $\frac{NH_3-N}{\text{Total N}}$	Sugar. By Citron.	Sugar. By rotation.
1908.		c. c.				gms.	gms.	gms.	p. ct.	gms.	gms.
July 13–14	....	Spec.	1035	ac.	Sl. +	..	....	..	....	..	[1]
July 15–16	....	1520	1041	ac.	+	7.1	....	1.5	....	..	103
July 16–17	....	2160	1038	ac.	+ +	..	....	2.0	....	..	121
July 17–18	....	2300	....	ac.	+ + +	..	....	..	....	..	138
July 19–20	....	2640	1034	ac.	+	..	....	..	....	..	137
Aug. 14–15	....	5000	1034	ac.	+ +	..	....	4.6	....	..	230
July 29–30	....	Spec.	1037	ac.	+ +	..	....	0.4	....	..	[2]
Sept. 1– 2	....	4250	1041	ac.	+ +	8.5	....	1.2	....	..	272
Sept. 13–14	....	2400	1031	ac.	+ + +	..	....	2.4	....	..	96
Sept. 14–15	....	3310[3]	1036	ac.	+ +	..	....	..	....	..	[3]126
Sept. 15–16	....	4540	1031	ac.	+ +	..	....	..	....	..	173
Sept. 16–17	....	4040	1030	ac.	+ +	..	....	..	....	..	129
Sept. 17–18	....	2670	1031	ac.	+ +	..	....	..	....	..	86
Sept. 18–19	....	2370	1033	ac.	+ +	..	....	..	....	..	100
Sept. 19–20	....	2745	1039	ac.	+ +	..	....	..	....	..	82
Sept. 20–21	....	3105	1027	ac.	+ + + +	..	....	3.9	....	..	80
Sept. 21–22	....	1830	1030	ac.	+ + +	..	....	..	....	..	44
Sept. 22–23	....	2085	1031	ac.	+ + +	..	....	4.2	....	..	42
Sept. 23–24	....	1680	1031	ac.	+ + +	..	....	..	....	..	30
Sept. 24–25	....	1875	1034	ac.	+ + + +	..	....	2.1	....	..	49
Sept. 25–26	....	1575	1028	ac.	+	..	....	..	....	..	3
Sept. 26–27	....	1860	1022	alk.	+ + +	..	....	..	....	0	..
Sept. 27–28	....	1710	1024	alk.	+ +	..	....	..	....	Tr.	0
Sept. 28–29	....	1740	1028	alk.	+ +	..	....	..	....	..	10
Sept. 29–30	....	1560	1031	alk.	Sl. +	..	....	..	....	..	22
Sept. 30–Oct. 1	....	1680	1030	alk.	+	..	....	..	....	..	13
Oct. 1– 2	....	1680	1031	alk.	+	..	....	..	....	..	7
Nov. 5– 6	....	....	1036	ac.	Sl. +	..	....	..	....	..	[4]
Nov. 6– 7	....	1920	1031	ac.	Sl. +	..	10.29	1.9	15.2	53	50
Nov. 7– 8	....	1905	1034	ac.	0	..	11.39	..	....	66	65
Nov. 8– 9	....	1440	1038	ac.	Sl. +	..	9.78	..	....	53	49
Nov. 9–10	....	1700	1037	ac.	Sl. +	..	22.11	..	....	63	58
Nov. 10–11	....	1720	....	....	....	..	22.42	..	....	58	58
Nov. 11–12	**F 1**	**972**	...	....	....	..	**16.29**	**1.7**	**8.6**	**27**	**23**
Nov. 12–13	**F 2**	**1946**	....	....	....	..	**29.31**	**2.1**	**5.9**	**73**	**73**
Nov. 13–14	....	....	....	....	....	..	....	..	....	..	..
Dec. 2– 3	....	3000	1036	alk.	Sl. +	..	....	..	....	..	102
1909.											
Jan. 11–12	....	2750	1033	ac.	+ +	..	....	..	....	99	77
Feb. 22–23	....	2000	1036	ac.	0	..	....	..	....	..	92
Apr. 20–21	....	2500	1038	ac.	Sl. +	..	....	..	....	..	150
May 3– 4	....	1250	1030	ac.	+ + +	..	....	..	....	28	..

[1] 7 per cent. [2] 6.8 per cent. [3] For 13 hrs. [4] 3.6 per cent.

EXPERIMENTS WITH CASE F.

Two metabolism experiments were conducted with this subject, both with the chair calorimeter. In the first, the metabolism after a 12-hours' fast, was studied, and in the second, after the ingestion of a large amount of protein. There were no respiration experiments made with this subject. The vital statistics were as follows:

Date of birth, September 16, 1885; height, 176 centimeters; body-weight, 59 kilograms.

TABLE 101.—*Clinical chart—Case F.*

Diet.						Carbohydrate-balance.	$NaHCO_3$.	Naked body-weight.	Remarks.
Carbohydrate.	Protein.	Nitrogen.	Fat.	Alcohol.	Calories.				
gms.	*gms.*	*gms.*	*gms.*	*gms.*		*gms.*	*gms.*	*kilos.*	
..	...	..	...	..	....	..	..	....	
..	...	..	...	..	....	..	..	....	
..	...	..	...	..	....	..	..	....	
..	...	..	...	..	....	..	..	....	
..	...	..	...	..	....	..	..	....	
..	...	..	...	..	....	..	..	....	
..	...	..	...	..	....	..	..	....	
..	...	..	...	..	....	..	..	....	
95	...	..	...	..	....	0	..	56.6	
115	...	..	...	..	....	..	12	56.4	
115	...	..	...	..	....	−60	12	55.8	
75	...	..	...	..	....	−55	12	54.9	
50	...	..	...	..	....	−35	12	54.8	
50	...	..	...	..	....	−50	12	55.0	
30	...	..	...	..	....	−50	12	55.6	Strict diet, vegetables, 500 c. c. cream, 9 gms. oatmeal.
30	...	..	...	..	....	−50	12	54.5	Do.
30	...	..	...	..	....	−15	20	54.6	Do.
30	...	..	...	..	....	−10	20	54.9	Do.
30	...	..	...	..	....	0	20	56.7	Do.
15	...	..	...	..	....	−35	20	57.2	Do.
10	...	..	...	..	....	+ 5	20	57.7	Vegetable day.
10	...	..	...	..	....	+10	20	57.2	Strict diet and vegetables in 5 per cent and 6 per cent groups.
10	...	..	...	..	....	+10	20	57.8	Do.
10	...	..	...	..	....	0	16	58.3	Do.
10	...	..	...	..	....	−10	12	57.4	The same and 30 c. c. cream.
10	...	..	...	..	....	− 5	12	58.1	Do.
10	...	..	...	..	....	+ 5	12	....	Do.
..	...	..	...	..	....	..	0	59.0	240 gms. meat, 4 eggs, 90 gms. cheese, 300 gms. vegetables, 75 gms. bread, 15 gms. oil, 120 gms. butter, 330 c. c. wine.
55	106	17	175	33	2500	..	0	58.3	
55	106	17	175	33	2500	..	0	58.3	Do.
55	106	..	175	33	2500	..	0	58.2	Do.
55	106	..	175	33	2500	..	0	58.2	Do.
55	106	..	175	33	2500	..	0	58.2	Do.
37	**78**	**12.5**	**150**	**21**	....	..	**0**	**57.9**	The same, minus 2 eggs, 45 gms. cheese, 30 gms. bread, 120 gms. wine.
37	**78**	**12.5**	**150**	**21**	....	..	**0**	**57.9**	Do.
40	113	18	225	24	2800	..	0	57.9	As Nov. 6-7 except omit bread and 90 gms. wine, and add 36 gms. oatmeal and 250 c. c. cream.
(?)	...	..	...	..	....	..	12±	....	
45	...	..	...	..	....	..	12±	....	
..	...	..	...	..	....	..	12±	....	
125	...	..	155	..	....	..	12±	....	Bread 210 gms., 180 gms. butter.
10	...	..	...	..	....	−20	12±	....	Vegetable day.

METABOLISM EXPERIMENT No. F 1.

Date, November 11, 1908. Naked body-weight, 59 kilograms.

As this experiment was designed to study the metabolism of a diabetic after a 12-hours' fast, the subject came to the laboratory without breakfast, and entered the calorimeter chamber at about 8 a. m. The experiment began at 8^h 50^m a. m. and continued for three 2-hour periods, ending at 2^h 50^m p. m. The subject drank no water while in the chamber. In an unsuccessful attempt to determine the oxygen consumption indirectly, the subject was weighed in a swinging chair at the beginning of every period and at the end of the experiment. In connection with the weighing, he was telephoned to several times, and the weighing and telephoning involved considerable muscular activity at times.[1] The subject reported that he was quite tired, but otherwise he found the conditions inside the chamber very comfortable.

The subject observed his own pulse-rate in 2-minute counts, the range for the experiment being from 80 to 82. He also made observations of his body-temperature with a clinical thermometer, sublingually, for the beginning of each period and at the end of the experiment. The results of the metabolism are given in table 102, and the statistics of the urine are given in table 104.

TABLE 102.—*Measurements of metabolism—Metabolism experiment No. F 1.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.[1]
November 11, 1908.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
8^h 50^m a.m. to 10^h 50^m a.m. .	48.9	46.6	207	272	38.5	0.76	180	[2]82
10 50 a.m. 12 50 p.m. .	47.5	45.6	202	266	58.7	.76	159	[3]81
12 50 p.m. 2 50 p.m. .	47.4	49.0	201	286	50.0	.70	155	80
Total 6 hours[4]	143.8	141.2	203	275	147.2	. . . .	[5]494	. .

[1] Pulse by the subject.
[2] Average of 2 records at 9 a. m. and 10 a. m.
[3] Average of 2 records at 11 a. m. and 12 noon.
[4] Carbon dioxide eliminated per kilogram per minute, 3.44 c. c.; oxygen absorbed per kilogram per minute, 4.66 c. c.; heat eliminated per kilogram per hour, 1.39 calories.
[5] Sublingual body-temperature at beginning, 37.00° C.; at end, 36.95° C. Heat production for total 6 hours, 491 calories.

Save for the abnormally high heat-elimination in the first 2 hours, the metabolism remained relatively constant throughout the whole experiment. There seems to be no apparent explanation for this larger elimination of heat, and as this was one of the first experiments with diabetics in this new apparatus, the technique had not been carried to such a degree of perfection as to have a perfect control of the whole apparatus. Consequently it is not surprising that one of these factors showed an abnormal value.

[1] Benedict, Am. Journ. Physiol., 1910, **26**, pp. 15–25. Benedict and Carpenter, Publication No. 123, Carnegie Institution of Washington, p. 93, 1910.

METABOLISM EXPERIMENT No. F 2.

Date, November 12, 1908. Naked body-weight, 59 kilograms.

In this experiment, which was carried out the day immediately following the fasting experiment, an attempt was made to study the influence of the ingestion of large quantities of protein on the metabolism of a diabetic. The subject came to the laboratory in the morning without breakfast and entered the calorimeter chamber at 8 a. m. Between $8^h 03^m$ a. m. and $8^h 35^m$ a. m. he ate 466 grams of beefsteak. The experiment began at $8^h 58^m$ a. m. and continued for three 2-hour periods, ending at $2^h 58^m$ p. m. He drank water at $10^h 35^m$ a. m. and $12^h 15^m$ p. m., the total amount being 229 c. c. He also used the telephone at the beginning of each period. After leaving the calorimeter chamber he stated that he felt all right, and that he noticed nothing abnormal about himself as a result of the experiment. He relished the steak, but said he could not have eaten a larger amount, and found it somewhat difficult to eat all that was given him.

The pulse-rate was taken in 2-minute counts by the subject himself and ranged from 86 to 90. The body-temperature measurements were also taken sublingually by the subject with a clinical thermometer for the beginning of each period and at the end of the experiment. The results of the metabolism are given in table 103. The statistics of the urine are given in table 104.

TABLE 103.—*Measurements of metabolism—Metabolism experiment No. F 2.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.[1]
			Carbon dioxide eliminated.	Oxygen absorbed.				
November 12, 1908.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
$8^h 58^m$ a.m. to $10^h 58^m$ a.m. .	59.7	59.0	253	344	42.3	0.74	199	[2]88
10 58 a.m. 12 58 p.m. .	59.8	58.2	254	340	66.6	.75	193	88
12 58 p.m. 2 58 p.m. .	57.4	57.6	244	336	46.1	.73	187	87
Total 6 hours[3]......	176.9	174.8	250	340	155.0	....	[4]579	..

[1] Pulse by the subject.
[2] Average of 2 records at $9^h 15^m$ a. m. and 10 a. m.
[3] Carbon dioxide eliminated per kilogram per minute, 4.24 c. c.; oxygen absorbed per kilogram per minute, 5.76 c. c.; heat eliminated per kilogram per hour, 1.64 calories.
[4] Sublingual body-temperature at beginning, 37.34° C.; at end, 36.89° C. Heat production for total 6 hours, 556 calories.

The metabolism during the first two periods, as indicated by the carbon-dioxide elimination, the oxygen consumption, and the heat-elimination, was essentially the same. There was a slight falling off of all three factors in the last period. Inasmuch as there was a noticeable decrease in the body-temperature as measured by the clinical thermometer, the heat-production is considerably lower than the heat-elimination, 556 calories as compared with 579 calories. It must be borne in mind, however, that the measurements by the clinical ther-

mometer under the tongue are too uncertain to make them absolutely reliable, and hence no special emphasis should be laid upon the heat-production in these experiments.

TABLE 104.—*Statistics of urine—Metabolism experiments Nos. F 1 and F 2.*

Date and period.	Quantity.	Total nitrogen.	Sugar.		D : N.
			Polarization.	Titration.	
November 11–12, 1908.	*grams.*	*grams.*	*grams.*	*grams.*	
7h 00m a.m. to 8h 50m a.m.	87	1.19	2.3	2.7	2.27
8 50 a.m. 10 50 a.m.	95	1.39	1.7	1.9	1.37
10 50 a.m. 12 50 p.m.	70	1.09	.6	.8	.73
12 50 p.m. 2 50 p.m.	55	.93	.1	.3	.32
2 50 p.m. 7 00 a.m.	665	11.69	18.6	21.6	....
November 12–13, 1908.					
7h 00m a.m. to 8h 58m a.m.	142	1.95	5.1	5.4	....
8 58 a.m. 10 58 a.m.	273	3.11	10.9	9.8	....
10 58 a.m. 12 58 p.m.	244	3.59	9.8	10.2	....
12 58 p.m. 2 58 p.m.	157	3.05	5.7	5.8	....
2 58 p.m. 7 00 a.m.	1130 c.c.	17.61	41.0	41.4	....

COMPARISON OF THE EXPERIMENTS WITH CASE F.

The two experiments are designed to compare the metabolism of the subject when without food and after eating considerable quantities of cooked beefsteak. An abstract of the results is given in table 105. There is a noticeable increase in the total metabolism as measured by the factors, carbon-dioxide elimination, oxygen-absorption, and heat-elimination and production following the ingestion of food, and the pulse-rate was also greater in the experiment with food. The respiratory quotient remained the same in both experiments. The discussion of the influence of the ingestion of protein on metabolism in diabetes will be considered in a subsequent portion of this report.

TABLE 105.—*Comparison of metabolism experiments with Case F.*

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute.		Respiratory quotient.	Heat eliminated per hour.	Heat produced per hour.	Average pulse per minute.
				Carbon dioxide eliminated.	Oxygen absorbed.				
		kilos.	*hrs.*	*c. c.*	*c. c.*		*cals.*	*cals.*	
F 1	Nov. 11, 1908	59	6	203	275	0.74	82	82	81
F 2	Nov. 12, 1908 [1]	59	6	250	340	.74	97	93	88

[1] 23 minutes before the experiment began, the subject finished eating 466 grams of cooked beefsteak.

GROUP I. CASE G.

DESCRIPTION OF THE CASE.

Male; born December, 1874; married; broker; came under our observation February 13, 1909, but his case had been closely studied for many years previously.

Family history.—No history of diabetes in the family. Father died at about 40 of tuberculosis; mother and six brothers living and well; one sister died of suppurative appendicitis. Several children, the last born spring, 1909.

Past history.—In 1891 severe pneumonia with thrombosis of the femoral vein. December, 1900, severe catarrhal jaundice. Urine December 4, 1900, free from sugar, but upon January 3, 1901, 1.3 per cent. The glycosuria disappeared at once on restriction of diet, and did not return after resumption of a liberal diet containing sugar.

Present illness.—December, 1904, right pyelo-nephritis, urine sugar-free; January 3, 1905, sugar appeared with a moderate amount of acetone, but no diacetic acid. The sugar persisted for 1 week, but disappeared on a diet of diluted cream, broth, and egg. The infection of the right kidney subsided after a week, to be followed after a few days by a much more serious infection and enlargement of the left kidney, which lasted for 6 weeks. Colon bacillus present in pure culture. Until July, 1906, able to eat freely of toast, oatmeal, potato, rice, or oranges without glycosuria, but any sugar or a single slice of untoasted bread caused it. Since July 24, 1906, see chart. In July, 1907, it was necessary to restrict protein to get sugar-free. In January, 1908, glycosuria disappeared only on hunger day, and acidosis was increasing. Since February, 1908, not sugar-free. The following green days illustrate the increase in the severity of the condition.

Date.	Sugar.	Nitrogen.	Ammonia.	Sodium bicarbonate.
	grams.	*grams.*	*grams.*	*grams.*
July 10, 1908....	29	13.6	1.1	0
Dec. 29, 1908....	48	....	1.0	45
Jan. 23, 1909....	100	15.9	3.7	30

Physical examination.—Weak. Height, 178 centimeters. Pupils equal and react, pulse regular, color good, knee jerks normal. Lungs and heart: nothing abnormal found. Abdomen: liver palpable two fingers' breadth below the costal margin, otherwise nothing else abnormal.

General history and treatment of case.—The patient entered the Corey Hill Hospital February 13, 1909, and during his stay there the diet was closely followed and all the experiments made. Subsequently his condition changed but little, save for a gradual loss of weight which was 58.1 kilograms in March, 1910.

The carbohydrates administered while in the hospital were in the form of bread, cream, and vegetables. The total amount was certainly much less than that to which the patient was accustomed. He acknowledged that previous to entering the hospital he had eaten rather more freely than usual of carbohydrates, though not as much as if he were on an unrestricted diet. The constancy of the minus carbohydrate-balance is good evidence of the care with which the details of diet were followed while in the hospital. The diet, however, was not sufficient for the patient's needs, for he steadily lost weight. Subsequent to leaving the hospital the diet was raised to somewhat over 100 grams of carbohydrates.[1] The history of the case is shown in the chart herewith (table 106).

The high volume of urine, ranging from 2784 c. c. to 4800 c. c., is evidently due, as in Case C, to acidosis as well as sugar, because the quantity of sugar excreted from February 13 to February 20 was not excessive. Albumen was absent throughout. The acidosis was extreme. The reaction of the urine was acid while at the hospital, although 30 grams of sodium bicarbonate were given daily. Large quantities of β-oxybutyric acid were excreted. In only one case, Case C, was so much eliminated from the body during 1 day. The especially large quantities, 55.3 grams and 51 grams, came on days following the first fasting experiment in the calorimeter when the quantity of carbohydrates was somewhat lowered.

The ammonia was nearly constant at 5 grams despite the large quantity of alkali administered. It is noteworthy, however, that the ammonia-nitrogen-nitrogen ratio was not nearly as high as would be expected from the total β-oxybutyric acid and ammonia.

The case as a whole is paricularly interesting from the therapeutic standpoint. It emphasizes the importance of prophylaxis even when glycosuria is most transitory. Further, the duration of life of the patient illustrates what careful medical treatment can accomplish in a severe case of diabetes. The patient throughout the course of the disease was under the care of Dr. Theodore C. Janeway.

EXPERIMENTS WITH CASE G.

Throughout these experiments the subject was in a nearby hospital and lived under hospital régime. Three metabolism experiments were made, one in the bed calorimeter and two in the chair calorimeter. Of these, the first was carried out after a 12-hours' fast, and without breakfast, the second after the ingestion of carbohydrates, and the third, after the ingestion of a considerable amount of protein. No respiration experiments were made with this subject. The vital statistics were as follows:

Date of birth, December, 1874; height, 178 centimeters; naked body-weight, 67.1 kilograms.

[1] Death occurred in coma, May, 1910.

TABLE 106.—*Clinical chart—Case G.*

Date.	Experiment No.	Volume of urine.	Specific gravity.	Diacetic acid.	β-oxybutyric acid.	Nitrogen.	Ammonia. Total.	Ammonia. $\frac{NH_3-N}{\text{Total N}}$	Sugar. By Citron.	Sugar. By rotation.	Diet. Carbohydrate.	Diet. Protein.	Diet. Nitrogen.	Diet. Fat.	Diet. Alcohol.	Diet. Calories.	Carbohydrate balance.	$NaHCO_3$.	Naked body-weight.
1906.		*c. c.*			*gms.*	*gms.*	*gms.*	*p. ct.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*		*gms.*	*gms.*	*kilos.*
July 24–25	......	3900	1010	....	....	.....	..	....	0	....	150	...	..	...	..	....	....	0	....
Oct. 29–30	......	....	1021	....	....	.....	..	....	trace	....	90	...	..	...	..	....	....	0	69.4
1907.																			
Jan. 6– 7	......	1530	1027	0	....	.....	..	....	16.8	....	40	...	..	...	..	....	....	0	70.7
Jan. 20–21	......	1560	1031	tr.	....	.....	..	....	39	....	50	...	..	...	..	....	....	0	70.7
Jan. 27–28	......	2000	1026	tr.	....	.....	0.8	....	12	....	..	...	..	...	..	....	....	0	69.2
Feb. 17–18	......	1700	1025	+	....	.....	..	....	18.7	....	..	...	..	...	..	....	....	0	70.6
Mar. 6– 7	......	1680	1027	0	....	.....	..	....	6.7	....	120	...	..	...	..	....	....	0	73.2
Apr. 24–25	......	1400	1026	+	....	.....	0	....	5.6	....	..	...	..	...	..	....	....	15	73.3
July 18–19	......	1230	1027	0	....	.....	0.9	....	0	....	..	...	..	...	..	....	....	0	68.2
Oct. 10–11	......	2280	1032	+ +	....	.....	..	....	70.6	....	20	...	..	...	..	....	....	0	70.1
Oct. 21–22[1]	......	2245	1035	+ +	....	.....	1.0	....	56.1	....	..	...	..	...	..	....	....	8	70.2
Oct. 30–31[2]	......	1380	1030	+	....	.....	0.4	17.6	11.4	....	..	...	..	...	..	....	....	8	71.5
Nov. 5– 6[2]	......	1290	1027	+ +	....	.....	1.5	....	6.4	....	90	...	..	...	..	....	....	8	71.4
1908.																			
Dec. 31–Jan. 1[2]	......	1960	1027	2.12	....	.....	2.4	15.8	35.3	....	135	...	..	...	..	....	....	8	69.9
Jan. 9–10[2]	......	1800	1027	1.75	....	.....	1.3	16.3	9.8	....	90	...	..	...	..	....	....	8	71.6
Jan. 29–30	......	2380	1030	....	....	14.95	0.8	....	2.4	0	15	...	12	...	..	....	....	8	66.2
Jan. 30–31[3]	......	1540	1021	....	....	10.01	0.6	....	0	0	0	...	2	...	..	....	....	..	65.5
Jan. 31–Feb. 1	......	1560	1030	....	....	14.65	0.4	....	0	—0.1[4]	15	...	12	...	..	....	....	..	66.3
Feb. 1– 2	......	1480	1028	....	....	14.72	0.7	....	1.5	0	15	...	13	...	..	....	....	8	66.3
Feb. 2– 3	......	2570	1019	....	....	16.71	0.7	....	5.1	+0.1[4]	15	...	13	...	..	....	....	8	66.2
Feb. 3– 4	......	2540	1019	....	....	14.26	0.7	....	10.2	+0.4[4]	50	...	13	...	..	....	....	8	65.7
Feb. 4– 5	......	1420	1030	....	....	12.23	0.5	....	8.5	+0.6[4]	50	...	14	...	..	....	....	8	65.8
Feb. 5– 6	......	2120	1029	....	....	17.79	0.6	....	21.2	1.0[4]	50	...	14	...	..	....	....	8	66.4
Feb. 6– 7	......	1900	1031	....	....	15.68	0.8	....	28.5	+1.5[4]	50	...	13	...	..	....	....	8	66.2
Feb. 7– 8	......	2290	1029	....	....	16.42	0.8	....	41.2	+1.8[4]	50	...	13	...	..	....	....	8	65.9
Feb. 8– 9	......	2360	1030	....	....	16.92	0.5	....	63.7	+2.6[4]	50	...	14	...	..	....	....	8	65.4
Feb. 9–10	......	2120	1032	....	....	16.42	0.6	....	53	+2.5[4]	50	...	14	...	..	....	....	8	65.4
Dec. 28–29	......	3190	1029	....	....	.....	1.0	....	47.8	+1.1[4]	50	...	..	...	..	....	....	..	65.4
1909.																			
Jan. 19–20	......	4020	1031	....	....	24.17	5.0	....	136.7	+2.9[4]	15	...	..	...	..	....	....	45	61.3
Jan. 22–23	......	3860	1027	....	....	15.90	3.7	....	100.4	+1.9[4]	20	...	..	...	..	....	....	15	63.0
Feb. 1– 2	......	4260	1027	....	....	14.11	3.0	....	102.2	+1.9[4]	20	...	..	...	..	....	....	15	62.7
Feb. 2– 3	......	4700	1030	....	....	13.43	1.4	....	159.8	+3.2[4]	95	...	..	...	..	....	....	15	64.6
Feb. 3– 4	......	4760	1030	....	....	13.43	1.0	....	185.6	+3.5[4]	95	...	..	...	..	....	....	15	65.4
Feb. 4– 5	......	4940	1027	....	....	12.10	1.1	....	153.1	+2.9[4]	95	...	..	...	..	....	....	15	65.2
Feb. 13–14[5]	......	1800	1031	+ + + +	....	.....	..	....	90	72	..	...	..	...	..	....	....	30	65.7
Feb. 14–15	......	3330	1029	+ + + +	36.8	17.1	4.5	21.7	134	107	55	106	17	177	30	2450	—79	30	63.8
Feb. 15–16	......	3180	1030	+ + +	36.8	18.9	4.7	20.5	124	95	55	106	17	177	30	2450	—77	30	64.5
Feb. 16–17	**G 1**	**2784**	**1031**	**+ + + + +**	**29.9**	**17**	**4.2**	**20.3**	**94**	**72**	**43**	**97**	**15**	**169**	**22**	**2250**	**–51**	**30**	**65.6**
Feb. 17–18	......	4410	1027	+ +	55.3	.....	4.9	....	133	....	56	100	16	220	30	2800	–78	30	64.8
Feb. 18–19	......	4800	1024	+ + +	51.0	17.2	4.9	23.5	134	77	73	88	14	208	30	2700	–72	30	63.6
Feb. 19–20	**G 2**	**3239**	**1023**	**+ + + +**	**17.6**	**13.6**	**3.8**	**23**	**155**	**104**	**80**	**62**	**10**	**130**	**15**	**1850**	**–75**	**30**	**63.6**

[1] Strict but much meat. [2] Strict with restricted proteid. [3] Hunger day. [4] Per cent. [5] For 13 hrs.

METABOLISM EXPERIMENT No. G 1.

Date, February 16, 1909. Naked body-weight, 67.1 kilograms.

The subject came to the laboratory in the morning without breakfast. Before entering the calorimeter chamber the lower bowel was emptied by a warm-water enema, and the subject entered the bed calorimeter at 8ʰ 23ᵐ a. m. The experiment began at 9ʰ 46ᵐ a. m. and continued for five 1-hour periods. Besides his regular clothing, the subject wore a heavy sweater and put on a pair of heavy socks over his ordinary ones, and low slippers, and covered the legs below the knees with a blanket. During the experiment he drank water as follows: 10ʰ 52ᵐ a. m., 200 c. c.; 12ʰ 36ᵐ p. m., 200 c. c.; 1ʰ 40ᵐ p. m., 200 c. c. The pulse-rate ranged from 69 to 74 and the respiration rate from 11 to 13. It was necessary for him to readjust the pneumograph at 12ʰ 12ᵐ p. m., as it was somewhat out of place. The subject remained quiet for the greater part of the time, the only activity being that incidental to urination, drinking water, etc. The subject said that he did not sleep during the experiment but he probably dozed at times. It is interesting to note that the evidence given by the pneumograph record is contrary to the statement furnished by the subject himself, who said that he was under intense nervous excitement throughout the whole experiment and found the sojourn inside the chamber distinctly disagreeable. As he expressed it, it seemed to him as if he must fly out through the walls of the chamber. Furthermore, neither the pulse nor the respiration-rates gave evidence of the intense nervous excitement which the subject claimed he experienced throughout the whole experiment. Judging from the pneumograph record, the muscular activity was about the same in all of the five periods.

The rectal thermometer indicated a rise in temperature from the beginning to the end of the experiment amounting to 0.31°, but as the calibration curve for this thermometer was not absolutely certain, the base line is not known with sufficient accuracy to report it. It is certain that the subject did not have a febrile temperature.

TABLE 107.—*Measurements of metabolism—Metabolism experiment No. G 1.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
February 16, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
9ʰ 46ᵐ a.m. to 10ʰ 46ᵐ a.m.	26.1	27.4	221	320	27.1	0.69	70	70	13
10 46 a.m. 11 46 a.m.	25.7	24.9	218	291	28.6	.75	75	71	13
11 46 a.m. 12 46 p.m.	26.6	27.9	226	326	31.0	.69	81	71	12
12 46 p.m. 1 46 p.m.	24.2	22.5	205	263	30.8	.78	85	71	12
1 46 p.m. 2 46 p.m.	24.5	23.2	208	271	31.0	.77	74	70	13
Total 5 hours[1]....	127.1	125.9	216	294	148.5	....	[2]385	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.22 c. c.; oxygen absorbed per kilogram per minute, 4.38 c. c.; heat eliminated per kilogram per hour, 1.15 calories.
[2] Rectal body temperature at the end was 0.31° C. higher than at the beginning. Heat production for total 5 hours, 401 calories.

The results for the metabolism and the average pulse- and respiration-rates are given in table 107. There was a noticeable decrease in the carbon-dioxide elimination in the fourth and fifth periods. This was accompanied by a decrease in the oxygen consumption. The irregularities in the respiratory quotient from period to period are in part explained by the points brought out in a previous discussion,[1] namely, that the oxygen determination for periods as short as 1 hour in the earlier experiments with this apparatus had not the significance that the carbon-dioxide determinations had, and hence only the average respiratory quotient for the whole experiment is of true significance. The heat-elimination was noticeably higher in the third and fourth periods than in any of the others. The respiration- and pulse-rates remained essentially the same throughout the whole experiment. In the third and fourth periods, the average values for the pulse- and respiration-rates are taken from a relatively few observations. The statistics for the urine are given in table 108.

TABLE 108.—*Statistics of urine—Metabolism experiment No. G 1.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
February 16–17, 1909.	c. c.		*grams.*	*grams.*	
$7^h 00^m$ a.m. to $9^h 46^m$ a.m.	219	1.030	1.12	8.4	7.50
9 46 a.m. 11 52 a.m.	250	1.029	1.35	8.4	6.22
11 52 a.m. 2 55 p.m.	433	1.020	2.02	7.4	3.66

METABOLISM EXPERIMENT No. G 2.

Date, February 19, 1909. Naked body-weight, 67.1 kilograms.

This experiment was designed to study the metabolism of a diabetic after the ingestion of carbohydrate food. The subject came from the hospital early in the morning and entered the chair calorimeter without breakfast. Between 8^h 19^m a. m. and 8^h 32^m a. m. he ate 75 grams of white bread and 25 grams of dextrose and drank 1 cup of clear, black coffee. The experiment began at 9 a. m. and continued for four 1-hour periods, ending at 1 p. m. Inasmuch as this subject experienced very disagreeable sensations in the bed calorimeter, the chair calorimeter was used for this experiment, and he found it much more agreeable. Water was consumed at the following times: 10^h 12^m a. m., 122 c. c., and 11^h 28^m a. m., 192 c. c. Shortly after the experiment began the subject was muscularly somewhat active in adjusting the cushion, and at 9^h 28^m a. m. he telephoned. The pulse- and respiration-rates were measured by the stethoscope and pneumograph, and the body-temperature by the electrical-resistance thermometer. The range in the pulse-rate was from 61 to 78, and the respiration-rate from 15 to 18.

The adjustment of the pneumograph was extremely unsatisfactory in this experiment. The subject was unusually quiet in the last period of the experiment.

[1] Benedict, Am. Journ. Physiol., 1910, **26**, p. 15.

The results of the metabolism and the average pulse- and respiration-rates are given in table 109. The carbon-dioxide excretion decreases regularly as the experiment progresses, there being a noticeable drop in the last period. The irregularities in the oxygen absorption and the values for the respiratory quotient are likewise quite considerable. The values for the pulse and respiration present nothing abnormal. The statistics for the urine are given in table 110.

TABLE 109.—*Measurements of metabolism—Metabolism experiment No. G 2.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
February 19, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
9 a.m. to 10 a.m.	25.7	20.9	218	244	20.3	0.90	90	71	16
10 a.m. to 11 a.m.	25.0	24.9	212	291	22.6	.73	90	73	17
11 a.m. to 12 noon	24.8	24.1	210	281	23.3	.75	92	69	17
12 noon to 1 p.m.	23.3	20.3	198	237	22.4	.84	83	69	17
Total 4 hours[1]	98.8	90.2	210	263	88.6	....	[2]355	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.13 c. c.; oxygen absorbed per kilogram per minute, 3.92 c. c.; heat eliminated per kilogram per hour, 1.33 calories.
[2] Rectal body temperature at beginning, 37.27° C.; at end, 37.42° C. Heat production for total 4 hours, 366 calories.

TABLE 110.—*Statistics of urine—Metabolism experiment No. G 2.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
February 19–20, 1909.	*c. c.*		*grams.*	*grams.*
$7^h 00^m$ a.m. to $9^h 00^m$ a.m.	325	1.028	1.19	13.2
9 00 a.m. 11 00 a.m.	581	1.028	1.37	30.8
11 00 a.m. 1 00 p.m.	347	1.028	1.08	16.9

METABOLISM EXPERIMENT No. G 3.

Date, February 20, 1909. Naked body-weight, 67.1 kilograms.

The subject came to the laboratory from the hospital in the morning, without breakfast, and entered the chair calorimeter at $8^h 05^m$ a. m. Between $8^h 12^m$ a. m. and $8^h 36^m$ a. m. he consumed 546 grams of cooked beefsteak. The experiment began at $8^h 54^m$ a. m. and continued for four 1-hour periods, ending at $12^h 54^m$ p. m. The water consumed during the experiment was as follows: $9^h 56^m$ a. m., 198 c. c.; $11^h 02^m$ a. m., 197 c. c.; and $12^h 24^m$ p. m., 192 c. c. The subject used the telephone at the end of each period.

The pulse- and respiration-rates were measured by the pneumograph and stethoscope, and ranged from 77 to 86 and from 13 to 20, respectively. The body-temperature was measured by the electrical-resistance thermometer. The subject stated that he was comfortable during the experiment, but that he was very glad to leave the calorimeter chamber as the confinement was very tedious.

Aside from the muscular movements incidental to urinating, drinking water, and telephoning, the subject remained for the most part sitting quietly.

The results of the metabolism and the average pulse- and respiration-rates are given in table 111. There was a noticeable increase in the carbon-dioxide production after the first period, which thereafter remained constant. There was likewise a marked increase followed by constancy in the oxygen consumption. On the other hand, the ratio of increase was such that the respiratory quotient remained essentially the same, being slightly decreased in the second period and increasing again in the third and fourth periods. The heat-elimination was the greatest in the fourth period. The average pulse-rate was the highest in the first period, and decreased to a constant value for the last three. The respiration-rate was slightly higher at the end of the experiment. The statistics for the urine are given in table 112.

TABLE 111.—*Measurements of metabolism—Metabolism experiment No. G 3.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
February 20, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
8h 54m a.m. to 9h 54m a.m.	26.9	25.8	228	301	29.0	0.76	96	84	16
9 54 a.m. 10 54 a.m.	31.1	31.9	264	372	30.8	.71	101	79	15
10 54 a.m. 11 54 a.m.	31.4	31.4	266	366	30.5	.73	100	78	17
11 54 a.m. 12 54 p.m.	31.1	30.1	264	351	32.4	.75	105	79	17
Total 4 hours[1].....	120.5	119.2	256	348	122.7	....	[2]402	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.82 c. c.; oxygen absorbed per kilogram per minute, 5.19 c. c.; heat eliminated per kilogram per hour, 1.51 calories.

[2] Rectal body temperature at beginning, 37.58° C.; at end, 37.77° C. Heat production for total 4 hours, 412 calories.

TABLE 112.—*Statistics of urine—Metabolism experiment No. G 3.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
February 20, 1909.	*c. c.*		*grams.*	*grams.*
6h 50m a.m. to 8h 54m a.m.......	191	1.034	1.15	9.6
8 54 a.m. 10 54 a.m.......	414	1.032	2.28	18.8
10 54 a.m. 12 54 p.m.......	339	1.032	2.70	15.4

COMPARISON OF THE EXPERIMENTS WITH CASE G.

Unfortunately, these three experiments are not strictly comparable, for the first experiment, which was the only one resting and without food, was made in the bed calorimeter, while the other two, which immediately followed the ingestion of food, were made in the chair calorimeter.

As will be seen in table 113 the carbon-dioxide excretion was unaffected by the ingestion of carbohydrate in the second experiment, and was noticeably increased by the ingestion of a large amount of meat in the third experiment. The

oxygen absorption actually decreased in the second experiment when carbohydrates were given, but increased enormously in the third experiment. The respiratory quotient, on the other hand, did increase somewhat during the carbohydrate experiment. The heat-elimination was larger in both experiments in the chair calorimeter than in the bed calorimeter, and much higher values were found in the experiment which followed the eating the beefsteak than in the experiment following the ingestion of carbohydrates. The pulse-rate was apparently affected only by the ingestion of meat, while the respiration-rate was much larger in the chair calorimeter than in the bed calorimeter.

TABLE 113.—*Comparison of metabolism experiments with Case G.*

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Respiratory quotient.	Heat eliminated per hour.	Heat produced per hour.	Average pulse-rate per minute.	Average respiration per minute.
	1909.	*kilos.*	*hrs.*	*c. c.*	*c. c.*		*cals.*	*cals.*		
G 1	Feb. 16[1]......	67.1	5	216	294	0.73	77	80	71	13
G 2	Feb. 19[2]......	67.1	4	210	263	.80	89	91	71	17
G 3	Feb. 20[3]......	67.1	4	256	348	.74	101	103	80	16

[1] Bed calorimeter.
[2] 28 minutes before the experiment began, the subject finished eating 75 grams of white bread and 25 grams of dextrose with 1 cup of clear black coffee.
[3] 18 minutes before the experiment began the subject finished eating 546 grams of cooked beefsteak.

It is much to be regretted that the experiments do not lend themselves to a better comparison. Since, however, with diabetics of this type the ingestion of carbohydrate food influences the metabolism but little, the experiment in which the carbohydrates were given (G 2) may be used for comparison with the experiment on the following day when steak was given. This will be treated in a subsequent section of this report.

GROUP I. CASE H.

DESCRIPTION OF THE CASE.

Female; born May 19, 1872; single; nurse; developed diabetes at 17 years of age; came under observation January 17, 1910.

Family history.—Father died of kidney trouble at 77; mother of diabetes mellitus at 47; one brother of diabetes mellitus at 21; one sister when about 17 years of age had sugar in the urine for 8 months, but is now 25 years old and somewhat undeveloped. Five brothers and sisters died as babies, one being a blue baby, and another dying of diphtheria. A brother and sister are well.

Past history.—Mumps; scarlet fever at 10; catamenia appeared at 11; never felt strong until 12, not going to school until 14; malaria for years while living near the Hudson River; later inflammatory rheumatism confining patient to bed; jaundice two or three times; gall stones twice.

Present illness.—At 17 years of age fearful thirst while at school. The urine was not measured, but the patient reports it as "heaps of urine." At 20 years of age dizziness, and sugar found in the urine by Dr. Stockton of Buffalo. Since this time the patient has been under the care of a great variety of excellent physicians on account of travel and occupation, and has undergone all sorts of treatment, both medicinal and dietetic. Despite her illness she went through a nurses' training school, and for the last 2 years has done an unusual amount of hard work, involving much responsibility and detail. The urine is said to have contained at one time 16 per cent of sugar, but investigation showed that the test used was not reliable. The greatest volume of urine observed by the patient was 180 ounces (5400 c. c.). The specific gravity is said to have been at one time 1060, and recently 1040. On March 5, 1904, the specific gravity was 1046; on March 21, 1043, and on March 28, 1904, 1042. When examined there was very little thirst, no fictitious appetite, and good digestion. The patient, however, had been troubled by exhaustion for 2 weeks, insomnia, headache, nausea and pain in the lumbar region, also in the hip and right knee. Eyesight troublesome. This winter the hands cracked and felt like sand paper, and there were callous spots on the feet, yet the patient said she felt "just as well as I can be."

Physical examination.—A healthy-looking young woman with red cheeks, but evidently rather tired out. Greatest weight, 60.8 kilograms; 1 year ago, 58.1 kilograms; January 17, 1910, 52.2 kilograms (all weights dressed). Height, 159 centimeters. Pulse, 100, regular. Blood-pressure, 140. Pupils equal and react; tongue moist and clear; teeth in good condition, as in Case I. No cervical, axillary, or inguinal glands. Hair slightly less than usual. A mass partly filling one-half of the right breast, which is hard, nodular, irregular, but it has been there for 5 or 6 years. Lungs and heart normal. Abdomen: nothing abnormal found; knee jerks normal.

General history and treatment of the case.—The case is remarkable because of the long duration. It is quite possible that this is due to the fact that there is a hereditary tendency. Recently attention has been called to the fact that hereditary cases of diabetes often are less virulent. Another case in our series (Case I) exemplifies this fact most strikingly, and still another case has been recently seen by us.

The carbohydrate-balance was positive until the carbohydrates were restricted from the neighborhood of 160 grams to about 100 grams. Then it at once became minus, and practically remained minus from that time on. It will be noticed that upon calorimeter days as a rule the carbohydrate-balance was better than upon the other days, both preceding and following. Is this due to the fact that upon the calorimeter days the patient is starved for two-thirds of the day, in reality going from 7 p. m. the previous night until 1 p. m. the calorimeter day without food?

TABLE 114.—*Clinical chart—Case H.*

Date.	Experiment No.	Volume of urine.	Specific gravity.	Diacetic acid.	β-oxybutyric acid.	Nitrogen.	Ammonia. Total.	Ammonia. $\frac{NH_3 - N}{\text{Total N}}$	Sugar. By Citron.	Sugar. By rotation.	Diet. Carbohydrate.	Diet. Protein.	Diet. Nitrogen.	Diet. Fat.	Diet. Alcohol.	Diet. Calories.	Carbohydrate-balance.	$NaHCO_3$.	Naked body-weight.
1910.		*c. c.*			*gms.*	*gms.*	*gms.*	*p. ct.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*		*gms.*	*gms.*	*kilos.*
Jan. 20–21	....	3620	1036	0	....	....	...	....	...	260	...	..	..	...	0	..	....	0	....
Jan. 21–22	....	....	1040	0	....	....	...	....	...	[2]	...	..	..	...	0	..	....	0	49.9
Jan. 22–23[1]	....	2040	1035	0	....	....	...	....	...	135	215	..	..	...	0	..	+80	0	49.2
Jan. 23–24	....	2295	1036	0	....	....	...	....	...	138	195	..	..	...	0	..	+55	0	49.7
Jan. 24–25	....	2880	1032	0	....	15.0	2.0	11.0	...	161	185	..	..	...	0	..	+25	0	49.6
Jan. 25–26	....	2460	1034	0	....	....	...	....	...	138	180	..	..	...	0	..	+40	0	50.1
Jan. 26–27	....	3000	1030	0	....	....	...	....	...	150	185	..	..	...	0	..	+35	0	50.6
Jan. 27–28	....	2820	1033	0	....	....	...	....	...	154	185	..	..	...	0	..	+30	0	50.3
Jan. 28–29	....	2820	1030	0	....	....	...	....	...	130	155	..	..	...	0	..	+25	0	50.5
Jan. 29–30	....	2700	1028	+	....	....	...	....	...	130	170	..	..	...	0	..	+40	0	51.5
Jan. 30–31[3]	....	2640	1027	0	....	9.98	2.4	19.8	126	121	155	..	..	220	0	..	+35	0	51.8
Jan. 31–Feb. 1	....	2730	1026	0	....	10.33	...	....	119	104	140	..	..	...	0	..	+35	0	51.7
Feb. 1-2	**H 1**	**2730**	**1025**	**0**	....	**11.63**	...	....	**96**	**87**	**130**	..	..	...	**0**	..	+45	**0**	**51.7**
Feb. 2– 3	....	2730	102	....	....	....	...	....	...	...	170	..	..	...	0	..	....	0	50.4
Feb. 3– 4	....	2730	102[illegible]	....	....	....	...	....	...	...	175	..	..	...	0	..	....	0	51.3
Feb. 4– 5	....	2730	102[illegible]	....	....	....	...	....	...	...	155	..	..	...	0	..	....	0	51.6
Feb. 5– 6	....	2700	1027	+	....	8.92	...	....	120	108	155	..	..	...	0	..	+45	0	52.1
Feb. 6– 7[4]	....	3300	1028	0	...	11.17	...	....	149	149	170	..	..	...	0	..	+20	0	52.2
Feb. 7-8[5]	**H 2**	**2660**	**1026**	**0**	....	**11.35**	...	....	**113**	**96**	**165**	..	..	...	**0**	..	**+70**	**0**	**52.2**
Feb. 8– 9[6]	....	3000	1029	+	....	11.86	...	....	151	126	100	..	..	...	0	..	—25	0	52.2
Feb. 9-10	**H 3**	**2185**	**1023**	**0**	**11**	**10.59**	**2.9**	**22.6**	**66**	**57**	**95**	..	..	...	**0**	..	**+40**	**0**	**52.8**
Feb. 10–11	....	2910	1026	0	....	12.34	2.7	18.0	106	93	65	..	..	...	0	..	—30	0	52.8
Feb. 11–12	....	2715	1026	0	....	12.63	...	....	100	65	45	..	..	...	0	..	—20	0	52.6
Feb. 12-13	**H 4-6**	**1725**	**1022**	Sl. +	**8.3**	**9.13**	...	....	**45**	**38**	**45**	..	..	...	**0**	..	**+ 5**	**0**	**53.0**
Feb. 13–14	....	2340	1024	Sl. +	....	9.75	3.0	25.3	77	70	45	..	..	...	0	..	—25	0	53.0
Feb. 16–17	....	2520	1027	....	....	11.62	...	....	114	101	60	..	..	...	0	..	—40	0	....
Feb. 20–21	....	2130	1023	+	....	10.16	...	....	59	47	(?)	..	..	...	..	..	....	0	....
Mar. 4– 5	....	3090	1023	+	....	14.65	...	....	102	...	...	..	..	...	..	..	....	..	53.3

[1] Carbohydrates given as bread, potato, cream, grapefruit, apple.
[2] 7.4 per cent.
[3] Oatmeal instead of part of the potato.
[4] 36 grams oatmeal, 500 c. c. cream, meat, egg, vegetables, 150 grams bread, 60 grams potato, ½ grapefruit, 1 apple.
[5] The same as on February 6-7, without grapefruit.
[6] 36 grams oatmeal, 500 c. c. cream, meat, egg, vegetables, 60 grams bread, 60 grams potato, ½ grapefruit.
[7] The same as on February 8-9, without grapefruit.

It will be noticed by the chart (table 114) that the amount of ammonia increased only from 2 grams to 3 grams between January 4–5 and February 13–14. This is not only interesting but important, because it shows that restriction of the diet did not cause a great increase in acidosis. This is generally considered to be the rule when so great a reduction in the diet has been made as in this case, namely, a reduction from about 200 grams to about 50 grams.

The general condition of the patient improved much under treatment. Despite the fact that she said she was in good condition at the start, she really was not, but was tired out and very nervous. As she underwent treatment her improvement was marked, and she herself volunteered that she felt better than she ever expected to feel again, also that her eyesight was much improved. This general improvement corresponds with the high respiratory quotient which she invariably showed.[1]

EXPERIMENTS WITH CASE H.

Five metabolism experiments were carried out with this subject, and one respiration experiment, all without food. The bed calorimeter was used for all the metabolism experiments. The vital statistics were as follows:

Date of birth, May 19, 1872; height, 159 centimeters; range of naked body-weight, 51.8 to 52.3 kilograms.

METABOLISM EXPERIMENT NO. H 1.

Date, February 1, 1910. Naked body-weight, 51.8 kilograms.

The subject came from the hospital to the laboratory without breakfast and entered the bed calorimeter at 8^h 06^m a. m. The experiment began at 9^h 05^m a. m. and continued for three 1-hour periods, ending at 12^h 05^m p. m. The pulse-

TABLE 115.—*Measurements of metabolism—Metabolism experiment No. H 1.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
February 1, 1910.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
9^h 05^m a.m. to 10^h 05^m a.m.	19.2	17.9	163	209	25.5	0.78	54	85	21
10 05 a.m. 11 05 a.m.	20.3	19.9	172	232	29.5	.74	70	84	21
11 05 a.m. 12 05 p.m.	19.9	20.1	169	235	30.0	.72	56	..	20
Total 3 hours[1]	59.4	57.9	168	225	85.0	....	[2]180	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.24 c. c.; oxygen absorbed per kilogram per minute, 4.34 c. c.; heat eliminated per kilogram per hour, 1.16 calories. The urine collected between 7 a. m. and 12^h 15^m p. m. amounted to 511 c. c. having a specific gravity of 1.023. It contained 1.70 grams of nitrogen and 16.9 grams of sugar, giving a D : N ratio of 9.94.

[2] Sublingual body temperature at beginning, 37.00° C.; at end, 36.72° C. Heat production for total 3 hours, 166 calories.

[1] On a trip to Europe in May, 1910, the patient became seasick, and after three days coma developed and death ensued.

and respiration-rates were measured by the pneumograph and stethoscope, and ranged from 81 to 88 and from 17 to 23, respectively. The rectal thermometer was not used in this experiment, the body-temperature measurements being taken sublingually by the subject with clinical thermometers.

In the second period the subject was very restless, but in the third period she was asleep the greater part of the time.

The metabolism measurements are given in table 115, together with the average pulse- and respiration-rates.

METABOLISM EXPERIMENT No. H 2.

Date, February 7, 1910. Naked body-weight, 52.3 kilograms.

The subject came to the laboratory in the morning without breakfast and entered the bed calorimeter at 8h 01m a. m. The experiment began at 9h 08m a. m. and continued for three 1-hour periods, ending at 12h 08m p. m. The pulse- and respiration-rates were measured as in the previous experiment with the stethoscope and pneumograph and ranged from 64 to 89 and from 13 to 23, respectively. The clinical thermometers were used for measuring the body-temperature which was taken by the subject sublingually. The temperature conditions inside the chamber were not wholly satisfactory, owing to the extreme cold weather at the time of the experiment. The subject remained fairly quiet throughout the experiment.

The measurements of the metabolism and the average pulse- and respiration-rates are given in table 116, and the statistics of the urine in table 117.

TABLE 116.—*Measurements of metabolism—Metabolism experiment No. H 2.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
February 7, 1910.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
9h 08m a.m. to 10h 08m a.m.	18.5	17.4	157	203	16.8	0.77	41	77	20
10 08 a.m. 11 08 a.m.	19.2	18.1	163	211	18.6	.77	53	78	18
11 08 a.m. 12 08 p.m.	19.2	16.8	163	196	20.5	.84	52	76	21
Total 3 hours [1].....	56.9	52.3	161	203	55.9	....	[2]146	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.08 c. c.; oxygen absorbed per kilogram per minute, 3.88 c. c.; heat eliminated per kilogram per hour, .94 calories.
[2] Sublingual body-temperature at beginning, 36.72° C.; at end, 36.67° C. Heat production for total 3 hours, 143 calories.

TABLE 117.—*Statistics of urine—Metabolism experiment No. H 2.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
February 7, 1910.	*c. c.*		*grams.*	*grams.*	
7h 00m a.m. to 12h 15m p.m.......	505	1.025	2.13	17.4	8.17
12 15 p.m. 7 00 a.m.......	2154	.....	9.22	94.9	....

METABOLISM EXPERIMENT No. H 3.

Date, February 9, 1910. Naked body-weight, 52.3 kilograms.

The subject came to the laboratory without breakfast and entered the bed calorimeter at $10^h\ 05^m$ a. m. The experiment began at $11^h\ 16^m$ a. m. and continued for three 1-hour periods, ending at $2^h\ 16^m$ p. m. The beginning of the experiment was delayed owing to difficulty with the stethoscope, which did not record. As the subject was unable to remedy the difficulty, it was decided to make the experiment without recording the pulse-rate. The respiration-rate was, however, obtained with the pneumograph and ranged from 13 to 25. The body-temperature measurements were obtained by means of clinical thermometers.

The first half of the first period, the subject was asleep, and also for the first 15 minutes in the second period. The last period she was awake apparently for most of the time.

The metabolism measurements for this experiment are given in table 118, as is also the average respiration-rate for the experiment. The statistics of the urine are given in table 119.

TABLE 118.—*Measurements of metabolism—Metabolism experiment No. H 3.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.				
February 9, 1910.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
$11^h 16^m$ a.m. to $12^h 16^m$ p.m..	17.6	15.1	149	176	22.6	0.85	52	20
12 16 p.m. 1 16 p.m..	18.1	16.9	154	197	24.2	.78	58	[1]20
1 16 p.m. 2 16 p.m..	18.9	16.9	160	197	24.2	.82	56	21
Total 3 hours[2]......	54.6	48.9	154	190	71.0	....	[3]166	..

[1] Two records in first half hour.
[2] Carbon dioxide eliminated per kilogram per minute, 2.94 c. c.; oxygen absorbed per kilogram per minute, 3.63 c. c.; heat eliminated per kilogram per hour, 1.05 calories.
[3] Sublingual body-temperature at beginning, 36.67° C.; at end, 36.45° C. Heat production for total 3 hours, 156 calories.

TABLE 119.—*Statistics of urine—Metabolism experiment No. H 3.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
February 9, 1910.	*c. c.*		*grams.*	*grams.*	
$7^h 00^m$ a.m. to $10^h 00^m$ a.m.......	274	1.022	1.12	8.2	7.32
10 00 a.m. 2 20 p.m.......	313	1.022	4.45	8.8	1.98

METABOLISM EXPERIMENT No. H 4.

Date, February 12, 1910. Naked body-weight, 52.3 kilograms.

The subject came to the laboratory as usual without breakfast and entered the chamber of the bed calorimeter at $9^h\ 04^m$ a. m. The experiment began at $10^h\ 03^m$ a. m., continued for only one 1-hour period, and was immediately followed by a respiration experiment. The pulse- and respiration-rates were obtained by means of the stethoscope and pneumograph, and ranged from 65 to 87 and from 18 to 21, respectively.

The measurements of the metabolism and the average pulse- and respiration-rates are given in table 120. The statistics of the urine are given in table 121.

TABLE 120.—*Measurements of metabolism—Metabolism experiment No. H 4.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
February 12, 1910.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$10^h 03^m$ a.m. to $11^h 03^m$ a.m.	19.3	19.4	[1]164	[1]226	22.5	0.72	[2]64	79	20

[1] Carbon dioxide eliminated per kilogram per minute, 3.14 c. c.; oxygen absorbed per kilogram per minute, 4.32 c. c.; heat eliminated per kilogram per hour, 1.22 calories.
[2] Sublingual body-temperature at $9^h 46^m$ a. m., 36.61° C.; at $10^h 46^m$ a. m., 36.50° C. Heat production for one hour, 59 calories.

TABLE 121.—*Statistics of urine—Metabolism experiment No. H 4.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
February 12, 1910.	*c. c.*		*grams.*	*grams.*	
$7^h 00^m$ a.m. to $9^h 15^m$ a.m.	150	1.021	0.76	4.1	5.40
9 15 a.m. 1 00 p.m.	355	1.020	1.81	8.0	4.42

METABOLISM EXPERIMENT No. H 5.

Date, March 5, 1910. Naked body-weight, 51.8 kilograms.

The subject came to the laboratory in the morning without breakfast and entered the chamber of the bed calorimeter at $8^h 18^m$ a. m. The experiment began at $9^h 10^m$ a. m. and continued for three 1-hour periods, ending at $12^h 10^m$ p. m. The pulse- and respiration-rates were taken with the stethoscope and pneumograph and ranged from 74 to 80 and from 21 to 24, respectively. The body-temperatures were measured as in previous experiments with the clinical thermometers, sublingually. At the end of the experiment, the subject said that the pneumograph was uncomfortably tight, but seemed to experience no other discomfort.

TABLE 122.—*Measurements of metabolism—Metabolism experiment No. H 5.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
March 5, 1910.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$9^h 10^m$ a.m. to $10^h 10^m$ a.m.	20.2	19.5	171	228	23.9	0.75	55	78	22
10 10 a.m. 11 10 a.m.	19.9	19.7	169	230	25.3	.73	59	75	23
11 10 a.m. 12 10 p.m.	18.2	16.3	154	190	24.4	.81	54	75	21
Total 3 hours[1].....	58.3	55.5	165	216	73.6	....	[2]168	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.19 c. c.; oxygen absorbed per kilogram per minute, 4.17 c. c.; heat eliminated per kilogram per hour, 1.08 calories. The urine collected between 6 a. m. and $12^h 45^m$ p. m. amounted to 880 c. c. having a specific gravity of 1.020. It contained 3.16 grams of nitrogen and 21.6 grams of sugar, giving a D : N ratio of 6.84.
[2] Sublingual body-temperature at beginning, 36.61° C.; at end, 36.61° C. Heat production for the total 3 hours, 168 calories.

During the first period, the subject was awake the greater part of the time, but near the end of the period, she fell asleep and slept during much of the second period. At the end of the second period, she was sound asleep and slept during practically all of the third period and until the end of the experiment.

The data regarding the metabolism measurements are given in table 122, together with the average pulse- and respiration-rates.

A comparison of the metabolism experiments are given in table 123.

TABLE 123.—*Comparison of metabolism experiments with Case H.*

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Respiratory quotient.	Heat eliminated per hour.	Heat produced per hour.	Average pulse-rate per minute.	Average respiration per minute.
	1910.	*kilos.*	*hrs.*	*c. c.*	*c. c.*		*cals.*	*cals.*		
H 1	Feb. 1.......	51.8	3	168	225	0.75	60	55	85	21
H 2	Feb. 7.......	52.3	3	161	203	.79	49	48	77	20
H 3	Feb. 9.......	52.3	3	154	190	.81	55	52	..	20
H 4	Feb. 12.......	52.3	1	164	226	.72	64	59	79	20
H 5	Mar. 5.......	51.8	3	165	216	.76	56	56	76	22

RESPIRATION EXPERIMENT NO. H 6.

Date, February 12, 1910. Naked body-weight, 52.3 kilograms.

This experiment followed a metabolism experiment of 1 hour in the bed calorimeter and included four periods, averaging about 15 minutes in length. The stethoscope and pneumograph were both used in this experiment, giving the pulse- and respiration-rates. The first period began after the nosepieces and surgeon's plaster had been adjusted 5 minutes. In the second period the respiration-rate was considerably more rapid than in the first period, and at the end of this period the right nosepiece was found to be defective and a new one was substituted before the third period was begun. A new set of nosepieces was also used for the last period. The results of the second period are not included in the tabulated data given in table 124.

TABLE 124.—*Results of respiration experiment No. H 6.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
February 12, 1910.	*m.* *s.*	*c. c.*	*c. c.*			
$11^h 32^m$ a.m.	15 2	162	209	0.78	77	7
12 18 p.m.	14 59	155	211	.74	80	13
12 56 p.m.	14 58	161	213	.76	78	12
Average		[1]159	[1]211	0.76	78	11

[1] Carbon dioxide eliminated per kilogram per minute, 3.04 c. c.; oxygen absorbed per kilogram per minute, 4.03 c. c.

GROUP I. CASE I.

DESCRIPTION OF THE CASE.

Male; born February 2, 1886; married; chauffeur; came under observation October 25, 1909.

Family history.—Father died of diabetes at age of 51, July 14, 1909, having been ill with the disease for 2 or 3 years. The immediate cause of death was appendicitis. One brother died of diabetes at the age of 11. Mother has gall stones. Two brothers and one sister well. The patient was married September, 1907, and has one child in fairly good health, five months old.

Past history.—A frail boy; scarlet fever, measles, chicken-pox, whooping cough. October, 1907, typhoid fever.

Present illness.—The date of onset is not accurately known, but during 1900 the patient was thirsty and rose several times at night to void urine. On May, 1902, sugar was found in the urine. Dr. Oscar O. Roberts, who examined the patient at that time, said that the indications were that sugar had been present for some time previous. Sugar was absent from the urine for a time in 1904, but has since been constantly present. Since the onset of the disease the patient has worked steadily, only occasionally losing some time, as during an attack of typhoid fever, and on account of a furuncle on the heel. He began his occupation as chauffeur in April, 1909. The present symptoms are most marked: Polydipsia, polyphagia, polyuria. The greatest quantity of urine noted in 24 hours was 12 quarts, and upon October 23, 1909, the quantity measured amounted to 10 quarts. The patient has a mania for ice-cream sodas. Up to the first of October the patient felt in fairly good health, but was then especially upset because he could not get the diet to which he had been accustomed, being forced to live while upon a visit chiefly on sugar and starch. He now eats "any time." No headache. He is recovering from a cough but has no sputum.

Physical examination.—The greatest weight, dressed, 60.8 kilograms; October 25, 1909, 49.5 kilograms, dressed; February, 1909, 53.5 kilograms. Height, 176 centimeters. Typical gaunt, flushed, dry appearance. Pupils equal and react; eyelids red; teeth in good condition; knee jerks normal; no edema; no cervical or axillary glands; but there are a few inguinal glands. Lungs and heart normal; pulse, 128; blood-pressure, 100; tongue red, back of tongue slightly dry. Abdomen: the liver and spleen were not felt, but the patient was ticklish. So-called acetone odor to breath. The whole room in which the patient passed the night of November 20, 1909, was filled with it. A student from the Harvard Medical School, who examined the patient, was suspected by his fellow-students later in the day of having the odor about him, and a peculiar odor was remarked by his friends.

General history and treatment of the case.—The history of the case may be seen by the chart herewith (table 125). Unfortunately, the data relating to diet, and even to the quantities of urine, are unreliable. This is suggested from

a study of the carbohydrate-balance, because it is almost inconceivable that it should vary so much in a few days, from being minus 120 grams on October 28 to 29 and positive 15 grams 4 days later, yet compare these data with the oatmeal days in Cases D and J.

TABLE 125.—*Clinical chart—Case I.*

Date.	Experiment No.	Volume of urine.	Specific gravity.	Diacetic acid.	Nitrogen.	Sugar.		Urine—Total Sugar.	Diet.		Carbohydrate-balance.[1]	$NaHCO_3$.	Naked body-weight.
						By Citron.	By rotation.		Carbohydrate.	Alcohol.			
1909.		*c. c.*			*gms.*	*gms.*	*gms.*		*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*
Oct. 23–24	......	10000	2039	0	....	...	680	..	...	..	...	..	....
Oct. 26–27[2]	......	3300	....	....	13.65	274	...	..	...	..	...	0	....
Oct. 27-28	**I 1**	**2855**	**1036**	**+**	**14.25**	...	**200**	..	**180**	..	**−20**	**0**	**47.0**
Oct. 28–29	......	5340	1032	+ +	23.5	...	288	..	170	7	−120	0	46.2
Oct. 29–30[3]	......	4090	....	....	17.11	...	...	..	150	7	...	45	48.3
Oct. 30-31	**I 2**	**4212**	**1029**	**+**	**12.99**	**118**	...	..	**80**	**15**	**−40**	**45**	**48.9**
Oct. 31–Nov. 1	......	5745	1026	+ + +	19.39	161	...	..	100	15	− 60	45	49.1
Nov. 1– 2	......	3630	1027	(?)	....	87	...	..	100	22	+ 15	45	48.3
Nov. 2– 3	......	3960	1028	+ + +	17.96	95	...	..	100	22	+ 5	40	48.6
Nov. 3– 4	......	3375	1029	Sl. +	....	98	...	..	100	22	0	40	47.9
Nov. 4– 5	......	4725	1032	+	....	198	...	..	80	22	−120	40	48.5
Nov. 5– 6[4]	......	3735	1029	+ +	....	134	...	..	90	22	− 45	40	48.6
Nov. 6– 7[4]	......	4980	1028	+	....	269	...	..	90	22	−180	40	48.6
Nov. 17–18[5]	......	3060	1034	+	....	...	202	..	...	..	...	..	....
Nov. 18–19	......	3120	1035	+ +	....	...	168	+	[6] 100	18	− 70	24	47.3
Nov. 19–20	......	3840	1032	Sl. +	....	...	...	+	...	18	...	24	48.2
Nov. 20–21	......	3660	1031	+ +	....	...	154	..	...	12	...	8	45.3
Nov. 21–22	......	1290	1031	+ +	....	...	41	..	...	18	...	24	....
Nov. 22–23	......	2640	1031	+ + + +	....	...	111	..	...	..	...	..	....

[1] Approximate.
[2] 15¼ hrs.
[3] October 30, a. m., looks and acts much better.
[4] Oatmeal day.
[5] For 12 hrs.
[6] Or less.

The reaction of the urine was acid throughout, although the patient was given 45 grams of sodium bicarbonate daily for 4 successive days, and 40 grams of sodium bicarbonate daily for 5 more days. The improvement of the patient when he took 45 grams of sodium bicarbonate on October 29 was striking. Evidently even the moderate restriction of diet changed his acidosis markedly, and the alkali gave him relief.

A very slight trace of albumen was present in the urine throughout the period of observation. The patient returned to the hospital November 17 saying that he felt better than he had felt for 2 years. The acetone odor was very marked. The patient was put upon a diet containing about 100 grams of carbohydrates, but it was not possible to determine just how much he ate of it. Certainly within a few days he changed greatly for the worse, so that there was considerable anxiety aroused as to his recovery. Upon November 21 his condition was so alarming that he was given chiefly oatmeal and milk, but it was difficult for him to take even this. He went home the following day. Some weeks later he was seen in a railroad station at 4 a. m. sleeping quietly and comfortably. On waking

he said that he had been very much used up on reaching home after his stay in the hospital, but that he had gradually regained strength, and was then feeling quite comfortable. He voided urine very frequently, but was able to do a little light work. Evidently the increase of carbohydrates which he must have had at home proved beneficial to him. It will be seen that the respiratory quotient was not as high in this case as in Case H, yet the average was somewhat higher than those of the other severe cases of diabetes.

EXPERIMENTS WITH CASE I.

Two calorimeter experiments were made with this subject, both in the chair calorimeter and both after 12-hours' fast and without breakfast. The subject was in a hospital at the time the experiments were made and living under hospital régime. The vital statistics were as follows:

Date of birth, February 2, 1886; height, 176 centimeters; range of naked body-weight, 45.1 to 45.3 kilograms.

METABOLISM EXPERIMENT NO. I 1.

Date, October 27, 1909. Naked body-weight, 45.1 kilograms.

The subject came to the laboratory in the morning at $8^h 15^m$ a. m. without breakfast. He was entirely unfamiliar with scientific investigations of this nature and had never seen the apparatus nor the laboratory before. He seemed to be very apprehensive and nervous. The apparatus and the purpose of the experiment were explained to him fully, then the pneumograph and stethoscope were adjusted. The subject found it impossible, however, to use the rectal thermometer, owing to an extremely small sphincter. Clinical thermometers were therefore used for measuring the body-temperature. The experiment began at $9^h 11^m$ a. m. and continued for two 1-hour periods, ending at $11^h 11^m$ a. m. The pulse-rate ranged from 114 to 130, and the respiration-rate from 15 to 24. After the experiment, the subject said that he was very hungry and weak, but otherwise the experience was not disagreeable.

TABLE 126.—*Measurements of metabolism—Metabolism experiment No. I 1.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
October 27, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$9^h 11^m$ a.m. to $10^h 11^m$ a.m.	23.3	22.2	198	259	31.6	0.76	76	124	20
10 11 a.m. 11 11 a.m.	22.6	21.5	192	251	30.3	.76	75	120	21
Total 2 hours[1].....	45.9	43.7	195	255	61.9	....	[2]151	...	..

[1] Carbon dioxide eliminated per kilogram per minute, 4.32 c. c.; oxygen absorbed per kilogram per minute, 5.65 c. c.; heat eliminated per kilogram per hour, 1.69 calories.
[2] Body-temperature at beginning, 36.95° C.; at end, 36.67° C. Heat production for total 2 hours, 139 calories.

For the most part the subject was very quiet during the experiment, and during the first period he was asleep for a few moments. Most of the time he sat reading or was sitting quietly unoccupied.

The results of the metabolism are given in table 126. The metabolism is strikingly uniform throughout the two periods with regard to all the factors, the carbon-dioxide eliminated, the oxygen consumed, and the heat eliminated. The average pulse-rate was very high, as was the respiration-rate. This did not necessarily indicate extreme nervousness on the part of the subject, for, as stated previously, he fell asleep during one of the periods, and as his normal pulse-rate is 120, the high pulse-rate would not be significant. The statistics of the urine are given in table 127.

TABLE 127.—*Statistics of urine—Metabolism experiment No. I 1.*

Date and period.	Volume.	Total nitrogen.	Sugar.	D : N.
October 27–28, 1909.	*c. c.*	*grams.*	*grams.*	
$3^h 45^m$ p.m. to $7^h 00^m$ a.m.	3300	13.65	273.6	....
7 00 a.m. 9 14 a.m.	131	.87	14.3	16.44
9 14 a.m. 10 14 a.m.	83	.57	....	....
10 14 a.m. 11 18 a.m.	93	.67	7.6	11.34
11 18 a.m. 12 27 p.m.	103	.75	....	....
12 27 p.m. 7 00 a.m.	2445	11.46	....	....

METABOLISM EXPERIMENT No. I 2.

Date, October 30, 1909. Naked body-weight, 45.3 kilograms.

As in the previous experiment the subject came to the laboratory in the morning without breakfast and entered the calorimeter chamber at $8^h 14^m$ a. m. The experiment began at $9^h 03^m$ a. m. and continued for three 1-hour periods, ending at $12^h 03^m$ p. m. The stethoscope and pneumograph were used in this experiment and an attempt was made to use the electrical-resistance thermometer. At $9^h 29^m$ a. m., however, the subject removed the rectal thermometer, which gave him considerable trouble. Aside from the disagreeable sensations occasioned by the rectal thermometer, which apparently annoyed him more than any other subject with whom we have experimented, he reported no discomfort as the result of the experiment.

The range in the pulse-rate was from 108 to 125, and the respiration-rate from 17 to 23.

The pneumograph did not keep in place during the whole experiment and there was considerable difficulty in properly adjusting it and securing an accurate record, as the subject was extremely thin and very tall. The subject was more restless during the first hour than at any other time. At $10^h 04^m$ a. m. he readjusted the pneumograph, and at $10^h 54^m$ a. m. there was also other muscular activity inside the chamber. The adjustment of the pneumograph was such that the amplitude of the respiration curve was much larger during the first period but the curve shows that the muscular activity was the least in the third period.

The data for the metabolism and the average pulse- and respiration-rates are given in table 128 herewith. The most pronounced features to be noticed in this table are the decrease in the oxygen absorption during the last period and the abnormally high pulse-rate throughout the whole of this experiment. The respiratory quotient averaged 0.72. The respiration-rate was likewise high, averaging 21. Both the pulse- and respiration-rates are the average of a large number of observations made in this experiment. The statistics of the urine are given in table 129.

TABLE 128.—*Measurements of metabolism—Metabolism experiments No. I 2.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
October 30, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
9h 03m a.m. to 10h 03m a.m.	23.4	24.2	199	282	25.6	0.70	76	123	21
10 03 a.m. 11 03 a.m.	23.5	23.8	199	278	27.0	.72	73	118	21
11 03 a.m. 12 03 p.m.	22.0	21.7	187	253	27.7	.74	71	112	21
Total 3 hours[1].....	68.9	69.7	195	271	80.3	....	[2]220	....	..

[1] Carbon dioxide eliminated per kilogram per minute, 4.31 c. c.; oxygen absorbed per kilogram per minute, 5.98 c. c.; heat eliminated per kilogram per hour, 1.61 calories.
[2] Sublingual body-temperature at 10h 03m a. m., 37.11° C.; at 12h 03m p. m., 36.84° C. Heat production for period 10h 03m a. m. to 12h 03m p. m., 130 calories.

TABLE 129.—*Statistics of urine—Metabolism experiment No. I 2.*

Date and period.	Volume.	Total nitrogen.
October 30–31, 1909.	*c. c.*	*grams.*
7h 00m a.m. to 10h 03m a.m........	457	2.07
10 03 a.m. 11 03 a.m.......	135	.63
11 03 a.m. 12 03 p.m........	170	.94
12 03 p.m. 7 00 a.m.......	3450	9.35

COMPARISON OF THE EXPERIMENTS WITH CASE I.

These two experiments, which were made within 3 days of each other and under the same conditions of nourishment, as may be seen from the hospital chart, furnish interesting proof as to the constancy of metabolism with such an individual under similar circumstances. A comparison of the two experiments given in table 130 shows that the carbon-dioxide excretion was identical in both experiments, but there was a slightly larger oxygen consumption in the second. On the other hand, the recorded figures for the heat-elimination show a somewhat greater heat-elimination during the first period, but the temperature data are insufficient for reading accurately the heat-production for the second experiment.

The respiratory quotient was somewhat lower in the second experiment than in the first, and the unusually high pulse- and respiration-rates are noticeable.

TABLE 130.—*Comparison of metabolism experiments with Case I.*

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute. Carbon dioxid eliminated.	Per minute. Oxygen absorbed.	Respiratory quotient.	Heat eliminated per hour.	Heat produced per hour.	Average pulse-rate per minute.	Average respiration per minute.
	1909.	*kilos.*	*hrs.*	*c. c.*	*c. c.*		*cals.*	*cals.*		
I 1	Oct. 27.......	45.1	2	195	255	0.76	76	70	122	20.5
I 2	Oct. 30.......	45.3	3	195	271	.72	73	..	118	21.0

General observations.—This subject was extremely high strung, nervous, and apprehensive. He had very small nostrils so that it was difficult and, indeed, impracticable to make respiration experiments with him with the small apparatus, and at the time these experiments were in progress the mouthpieces had not been adjusted so that we could use the mouth in breathing for making the determinations. The very small sphincter also made the use of the rectal thermometer very unsatisfactory. The subject was not an ideal subject, therefore, for experiments of this kind but it was hoped that some evidence might be secured as to his metabolism which would possibly assist in the dietetic treatment of his case.

GROUP I. CASE J.

DESCRIPTION OF THE CASE.

Male; born March 26, 1889; single; no occupation; came under observation September 24, 1909.

Family history.—No family history of diabetes. Father, mother, one brother, and one sister well.

Past history.—Measles, whooping cough, and possibly chorea at seven.

Present illness.—The present illness began in February, 1908, after an attack of influenza. Frequent micturition, polyuria, polydipsia, and weariness were noticed. Sugar was found in the urine 10 days later and persisted until November 17, 1909; since then it has been absent most of the time. The patient complained of no other symptoms, but cried during the physical examination.

Physical examination.—Height, 171 centimeters; greatest weight, fall of 1907, 62.6 kilograms; February, 1908, 61.3 kilograms; March, 1908, 56.7 kilograms; June, 1909, 62.6 kilograms; September 24, 1909, 57.8 kilograms. Pupils equal and react, knee jerks present, lungs normal. Heart extended 3 centimeters to the right of the median line and 10 centimeters to the left of the median line. A systolic murmur at the base. Pulse, 108; blood-pressure, 105 (Riva Rocci). No acetone odor to the breath. Abdomen, nothing abnormal felt. No edema.

General history and treatment of the case.—The course of the case is shown in the chart herewith (table 131).

TABLE 131.—*Clinical chart—Case J.*

Date.	Experiment No.	Volume of urine.	Specific gravity.	Reaction.	Diacetic acid.	Nitrogen.	Ammonia. Total.	Ammonia. $\frac{NH_3-N}{Total\ N}$	Sugar. By Citron.	Sugar. By rotation.
1909.		*c. c.*				*gms.*	*gms.*	*p. ct.*	*gms.*	*gms.*
Sept. 23–24	......	....	1037	ac.	+ +	....	....	....	+	4.4[1]
Sept. 26–27	......	....	....	....	....	....	....	....	..	....
Sept. 27–28	......	1950[2]	....	ac.	+ +	....	....	....	..	57[2]
Sept. 28–29	......	1860	....	....	....	....	....	....	..	37
Sept. 29–30	......	2820	....	....	+	....	....	....	..	68
Sept. 30–Oct. 1	**J 2**	**2580**	**1025**	ac.	+ +	....	....	....	..	**46**
Oct. 1– 2	......	3090	1022	ac.	+	....	....	....	..	43
Oct. 2– 3	......	2430	1019	ac.	+ +	....	....	....	..	39
Oct. 3– 4	......	2520	1022	ac.	+	....	....	....	..	55
Oct. 4–5	**J 3**	**1830**	....	....	Sl. +	....	....	....	..	**29**
Oct. 5– 6	......	2400	1022	ac.	+ +	11.0	....	....	..	48
Oct. 6– 7	......	2100	1021	ac.	+ +	....	....	....	..	42
Oct. 7– 8	......	2580	1021	ac.	+	....	....	....	..	44
Oct. 8– 9	......	2340	1027	ac.	+ +	....	....	....	..	61
Oct. 9–10	......	3000	1028	ac.	+ + +	....	....	....	..	72
Oct. 10–11	......	2640	1032	ac.	+ + +	....	....	....	..	74
Oct. 11–12	......	2940	1026	ac.	+ + + +	....	....	....	29	....
Oct. 12–13	......	3540	1015	Sl.ac.	+	....	....	....	39	....
Oct. 13–14	......	3360	1023	ac.	+	....	....	....	64	....
Oct. 14–15	......	2880	1022	ac.	+	....	....	....	25	....
Oct. 15–16	......	3240	1023	ac.	+ +	....	....	....	32	....
Oct. 16–17	......	2580	1027	ac.	+ + +	....	....	....	32	....
Oct. 17–18	......	3780	1028	ac.	+ +	....	....	....	91	....
Oct. 18–19	......	4110	1020	ac.	+ +	....	....	....	66	....
Oct. 19–20	......	3300	1024	ac.	+ +	....	....	....	43	....
Oct. 20–21	......	4320	1024	ac.	+ +	....	....	....	48	....
Oct. 21–22	......	2340	1031	ac.	+ + + +	....	....	....	42	....
Nov. 16–17	......	....	1020	alk.	+	....	....	....	tr.	0
Nov. 25–26	......	3000	1016	ac.	+ +	....	....	....	tr.	....
Nov. 30–Dec. 1	......	2580	1024	alk.	+	....	....	....	8	....
Dec. 16–17	......	2700	1017	ac.	0	....	....	....	11	....
1910.										
Jan. 5– 6	......	2400	1018	ac.	0	....	....	....	tr.	[1]— 0.1
Jan. 25–26	......	1620	1016	ac.	0	....	....	....	tr.	....
Feb. 16–17	......	2190	1022	ac.	+	17.0	2.8	13.6	..	35

[1] Per cent.
[2] First day's urine was for 23 hrs., but the total quantity sugar has been estimated for 24 hrs.

TABLE 131.—*Clinical chart—Case J.*

Diet.				Carbohydrate-balance.	NaHCO$_3$.	Naked body-weight.	Remarks.
Carbohydrate.	Protein.	Fat.	Alcohol.				
gms.	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*	
..	..	....	..	....	..	....	
..	..	....	..	....	..	52.4	
30	..	....	0	— 25	0	52.0	Strict diet, 250 c.c. cream, 18 gms. oatmeal, vegetables.
30	..	....	0	— 5	0	52.4	Do.
30	..	....	0	— 40	0	52.2	Do.
16	**50**	....	**0**	**—30**	**0**	**52.1**	Strict diet, but eggs limited to 3 and meat limited to 90 gms., 250 c. c. cream, vegetables.
16	50	200	0	— 30	0	51.5	The same, butter from now on 150 gms. daily.
16	50	200	6	— 25	0	51.7	The same, 60 gms. Zeltinger.
16	40	200	6	— 40	0	52.3	The same, meat limited to 60 gms.
16	**40**	**200**	**6**	**—15**	**0**	**52.0**	The same. Vomited. Later 150 gms. milk but not repeated.
16	25	200	12	— 30	0	51.7	120 gms. Zeltinger, idem, but no meat and yolks only of 4 eggs.
16	25	200	12	— 25	0	51.9	Do.
16	90	200	12	— 30	0	51.9	Strict diet, 4 eggs, 240 gms. meat, 30 gms. cheese, 250 c. c. cream, vegetables.
40	95	200	12	— 20	0	52.2	The same, except 2 eggs omitted and 500 gms. milk added.
40	95	200	6	— 30	32	52.4	The same, wine diminished to 60 gms.
19	80	200	6	— 55	32	53.1	Strict diet, 2 eggs, 240 gms. meat, 30 gms. cheese, 375 gms. cream, vegetables.
13	15	255	6	— 15	32	53.8	Vegetable day, 300 gms. butter, 90 c. c. cream, broths.
120	30	150	9	+ 80	32	52.9	Oatmeal day, 180 gms. oatmeal, 165 gms. butter, 90 gms. Zeltinger.
180	50	270	9	+115	32	53.3	270 gms. oatmeal, broths, coffee, 90 gms. Zeltinger, 320 gms. butter, oatmeal day.
13	70	200	9	— 10	32	54.1	Strict diet, 200 gms. meat, 3 eggs, 120 c. c. cream, 90 gms. wine, 165 gms. butter, vegetables.
16	70	230	9	— 15	32	53.8	The same, but 250 c. c. cream, 200 gms. butter.
16	70	210	9	— 15	32	54.2	The same, except 180 gms. butter.
180	50	180	9	+ 90	32	54.1	270 gms. oatmeal, 180 gms. butter, 120 gms. cream, 90 gms. wine, broths, coffee, tea.
180	50	180	9	+120	32	53.8	The same, oatmeal day.
16	70	230	9	— 25	32	54.3	Strict diet, 150 gms. meat, 30 gms. cheese, 4 eggs, 180 gms. butter, 90 gms. wine, 250 gms. cream, vegetables.
16	70	240	9	— 30	32	54.0	Strict diet, 210 gms. meat, 3 eggs, 195 gms. butter, 90 gms. wine, 250 c. c. cream, vegetables.
16	70	230	9	— 25	32	53.7	Strict diet, 180 gms. meat, 3 eggs, 30 gms. cheese, 180 gms. butter, 90 gms. wine, 250 c. c. cream, vegetables.
16	..	....	9	+ 15	24±	56.7	Strict diet, 250 c. c. cream, 90 gms. wine, 30 gms. oil.
16	..	....	6	+ 15	16	....	Strict diet, 250 c. c. cream, 60 gms. wine, 30 gms. oil, diarrhea.
16	..	....	6	+ 10	0?	....	Do.
16	..	....	6	+ 5	0?	56.7	Do.
20	..	....	6	+ 20	0	....	The same and ½ grapefruit.
20	..	....	6	+ 20	0	....	Do.
25	85	....	6	— 10	0	....	240 gms. meat, 3 eggs, ½ grapefruit, 250 c. c. cream, 90 gms. milk, 60 gms. wine, 300 gms. vegetables.

Albumen was absent from the urine throughout or present in only a very slight trace. The examination of a single specimen of urine of this patient upon September 24, before treatment was begun, shows the severity of the case. Diacetic acid was present, and yet there was 4.4 per cent of sugar. The diet at this time was probably fairly liberal, yet in spite of it diacetic acid was present. When first seen the aspect of the case suggested that the sugar would quickly disappear, because the minus carbohydrate-balance at first decreased, but to our surprise it did not disappear, but rather tended to remain stationary. At first a restriction of carbohydrates was made without effect. The patient, in fact, was on about as low a carbohydrate diet as is often used, namely, 300 grams vegetables and 250 c. c. cream. When this expedient failed, the protein was lowered. At the start this had not been very high, but it was gradually restricted to 25 grams, and yet upon this diet no marked change in the quantity of carbohydrates excreted was noted. Fearing to draw longer upon body protein, the patient was put upon a liberal amount of protein, and an experiment tried by giving 500 c. c. milk in addition to the former diet. The extra quantity of milk sugar was at once excreted. It is of interest to observe that the increased quantity of sugar, following the administration of the 500 grams of milk, continued for 1 day after the milk was omitted.

The patient was then put upon a vegetable day. He was remarkably adapted for such a day, because he was able to take large quantities of butter. On this day, for example, he used 300 grams. No patient who has ever come under our observation was able to take butter more readily. There was a quick reaction to the vegetable day, and the carbohydrates fell to as low a point as hitherto reached. It was followed by two oatmeal days with striking results. Although there had been a minus carbohydrate-balance from September 28 up to October 12, inclusive, under oatmeal it at once changed to a positive carbohydrate-balance of 80 and 115 grams, respectively. There was no material change in weight, although a slight increase was registered. The oatmeal days were borne satisfactorily. The quantity of diacetic acid decreased. Following these days the diet consisted of 16 grams carbohydrates, 70 grams protein, and about 230 grams fat. Upon this the quantity of sugar excreted was lower than had usually been the case up to this time, but a minus carbohydrate-balance at once appeared. The good effect of the oatmeal encouraged us to repeat its use, and with equally good result. Following this, however, upon the diet of 16 grams carbohydrates, 70 grams protein, and about 230 grams fat, the minus carbohydrate-balance reappeared, and persisted until the patient left the hospital, October 22.

The outcome of the case was considered doubtful, but the patient at his home continued most faithfully to follow out a carefully restricted diet with moderate protein and excessive amount of fat. It will be seen that gradually the minus carbohydrate-balance turned to a positive one, and at the same time the weight steadily increased. Finally, about 1 month after his return home sugar entirely disappeared and he remained practically sugar-free although one-half a grape-

fruit was allowed. Milk (90 grams) was then added with the reappearance of the sugar. The patient was sugar-free upon January 26, 1910, but 35 grams were present February 23, 1910.

The bulk of the diet of this patient was extremely small, and upon reading what he was given at the hospital, or on watching him eat, it appeared that he took a very small quantity of food. This, however, was not the case if we compare the caloric value of the diet and the weight of the patient while at the hospital. It will be seen that he had approximately 40 calories per kilogram.

EXPERIMENTS WITH CASE J.

One metabolism experiment in which the chair calorimeter was used was carried out with this subject, and prior to this, three respiration experiments. The experiments in all cases were made without food after a 12-hours' fast. The vital statistics were as follows:

Date of birth, March 26, 1889; height, 171 centimeters; range in naked body-weight, 52.3 to 54 kilograms.

METABOLISM EXPERIMENT No. J 1.

Date, October 22, 1909. Naked body-weight, 53.7 kilograms.

The subject came to the laboratory in the morning, without breakfast, and entered the chair calorimeter. The experiment proper began at $9^h 02^m$ a. m. and continued for three 1-hour periods, ending at $12^h 02^m$ p. m. The subject drank 200 c. c. of water during the first period, and the same amount during the second period.

The pulse- and respiration-rates were obtained by means of the stethoscope and pneumograph, and ranged from 79 to 90 and from 14 to 17, respectively. The body-temperature was taken by the subject with clinical thermometers under the tongue.

For the most of the experiment the subject sat quietly in the chair, excepting when telephoned to at the beginning of each period, and during urination. Toward the end of the second period he was somewhat restless. The greatest muscular activity was experienced in the last period, and the least in the first period. As this subject was of a nervous temperament the enforced quiet incidental to sitting in the chair doubtless caused a greater nervous tension and more activity as the experiment progressed.

The results of the metabolism are given in table 132, and the urine data in table 133. The carbon-dioxide excretion was lowest in the first period and constant in the last two periods. The oxygen absorption was somewhat larger in the second period, and the respiratory quotient for the three periods averaged 0.75. In this experiment, as in many others, the heat-elimination did not follow the course of either the oxygen absorption or the carbon-dioxide elimination. Thus the highest oxygen absorption was during the second period, while the heat-elimination in this period was the lowest. The course of the pulse and

respiration indicates a slightly increased muscular activity as the experiment progressed. On the whole, the three periods represent reasonably accurate experimental periods. The average of the experiment as a whole should indicate very closely the metabolism of this individual under the conditions existing when the experiment was made.

TABLE 132.—*Measurements of metabolism—Metabolism experiment No. J 1.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
October 22, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
9h 02m a.m. to 10h 02m a.m.	22.9	22.1	194	258	39.3	0.76	75	84	15
10 02 a.m. 11 02 a.m.	23.9	24.3	203	284	38.4	.72	70	88	16
11 02 a.m. 12 02 p.m.	23.9	22.7	203	265	36.8	.77	74	87	16
Total 3 hours[1].....	70.7	69.1	200	269	114.5	0.75	[2]219	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.72 c. c.; oxygen absorbed per kilogram per minute, 5.01 c. c.; heat eliminated per kilogram per hour, 1.36 calories.
[2] Body-temperature at beginning, 37.11° C.; at end, 36.94° C. Heat production for total 3 hours, 211 calories.

TABLE 133.—*Statistics of urine—Metabolism experiment No. J 1.*

Date and period.	Volume.	Total nitrogen.	Sugar.	D : N.
October 22, 1909.	*c. c.*	*grams.*	*grams.*	
7h 00m a.m. to 10h 04m a.m.......	337	1.02	5.1	5.00
10 04 a.m. 12 04 p.m.......	408	1.48	4.8	3.24

RESPIRATION EXPERIMENT No. J 2.

Date, September 30, 1909. Naked body-weight, 52.3 kilograms.

For this experiment the subject came to the laboratory without food. The experiment consisted of three periods, which averaged about 15 minutes in duration. All three periods showed an unusually high respiratory quotient for a diabetic, and subsequent experiments with this subject indicate that this might be due to errors in the determination of the oxygen consumption. If this is the case it is a striking illustration of the impracticability of relying upon duplicate experiments, for we have here three periods following each other rapidly which give duplicate results with the same subject, and in which the respiratory quotient is consecutively 0.89, 0.88, and 0.88. It seems impossible that the subject at this stage of his disease could have a respiratory quotient as high as indicated, and subsequent experiments showed that it might be higher than would be expected from the clinical features shown by this case. The pulse-rate was somewhat high during the first experiment and the respiration-rate averaged about 11. The results of the experiment are given in table 134.

TABLE 134.—*Results of respiration experiment No. J 2.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
September 30, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
$8^h 56^m$ a.m.	15	3	207	232	0.89	74	11
9 22 a.m.	15	2	201	228	.88	75	11
9 43 a.m.	15	0	222	253	.88	78	12
Average			210	238	0.88	76	11

RESPIRATION EXPERIMENT No. J 3.

Date, October 4, 1909. Naked body-weight, 52.3 kilograms.

The subject came to the laboratory in the morning and lay down on the couch for some 20 minutes before the experiment began. In this experiment, which consisted of five separate periods, it was possible to obtain the carbon-dioxide production in four periods, and the oxygen consumption in two. The results are given in table 135.

TABLE 135.—*Results of respiration experiment No. J 3.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
October 4, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
$8^h 40^m$ a.m.	14	52	208	253	0.82	65	10
9 09 a.m.	14	48	191	...	....	63	13
9 36 a.m.	14	34	213	...	....	68	12
10 01 a.m.	14	19	214	242	.88	69	13
Average			207	248	0.85	66	12

The urine collected between 7 a. m. and $10^h 15^m$ a. m. amounted to 443 c. c. and contained 1.19 grams of nitrogen and 6.0 grams of sugar, giving a D : N ratio of 5.04.

Of special significance is the high respiratory quotient again found with this subject. The pulse-rate was considerably lower than in the first experiment and the respiration-rate was somewhat higher. The carbon-dioxide production was about the same in both experiments.

RESPIRATION EXPERIMENT No. J 4.

Date, October 21, 1909. Naked body-weight, 54 kilograms.

This was the last attempt to make respiration experiments with this subject, and although there were five periods in this experiment, only two were successful; the results of these two are given in table 136, and the data for the urine in table 137.

The oxygen consumption was essentially the same as in the other experiments, and the carbon-dioxide elimination was somewhat lower. The respiratory quo-

tient still continued somewhat high for as severe a case of diabetes as that described by the clinical picture, being 0.76 and 0.77, respectively. The pulse-rate was essentially the same as that of the first experiment and the respiration-rate likewise.

A comparison of these three respiration experiments, therefore, shows that the most striking feature is the high respiratory quotient in the first two experiments, and the appreciable fall in the respiratory quotient in the third. The total metabolism, as measured by the oxygen intake, is not materially different in the three experiments. There is a noticeable decrease in the carbon-dioxide production in the last experiment, due to the combustion of a larger proportion of fat.

TABLE 136.—*Results of respiration experiment No. J 4.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
October 21, 1909.	m. s.	c. c.	c. c.			
$9^h 02^m$ a.m.	15 7	189	248	0.76	73	11
9 29 a.m.	14 58	186	241	.77	77	12
Average		188	245	0.77	75	11

TABLE 137.—*Statistics of urine—Respiration experiment No. J 4.*

Date and time.	Volume.	Total nitrogen.
October 21, 1909.	c. c.	grams.
$7^h 00^m$ a.m. to $9^h 47^m$ a.m.	490	1.01
9 47 a.m. 10 25 a.m.	325	.74

COMPARISON OF METABOLISM AND RESPIRATION EXPERIMENTS WITH CASE J.

Comparing the results of the respiration experiments with the metabolism experiment on the day following the last respiration experiment, we find a close agreement between the values in the last respiration experiment and in the metabolism experiment. There is a somewhat higher carbon-dioxide elimination and a slightly higher oxygen absorption, as would be expected from the difference in body-position and the increased muscular activity. On the other hand, the respiratory quotient is substantially the same in both experiments, thus verifying the respiratory quotient as determined by the two forms of apparatus. As may be expected, the pulse- and respiration-rates were considerably higher in the metabolism experiment inside of the respiration chamber, as compared with the respiration experiment on the day before.

The abnormally high respiratory quotients found with this subject in the first two respiration experiments are difficult to explain. It seems almost incredible that three periods following each other so closely as those in the first experiment

should give such remarkably constant respiratory quotients and an error be constant throughout. From a critical examination of the apparatus and technique, no cause for such an error was apparent. Furthermore, as a matter of fact, it has been found that usually the greatest errors occur through the measurement of excessive volumes of oxygen, which would tend to result in an abnormally low rather than an abnormally high respiratory quotient. Every precaution to avoid such errors was taken in all of these experiments, although the nervous temperament of the subject and his unwillingness to cooperate with us to the fullest extent made it extremely difficult to interpret these results. The values for the respiratory exchange in the two first respiration experiments, therefore, must be considered with some reserve. From an examination of the history of the case and the clinical picture, together with the charts and the dietetic régime, it would seem impossible that a respiratory quotient of this value could be found with a subject suffering from so severe a case of diabetes. On the other hand, as has been previously stated, it was impossible to detect an error either in the technique or in the manipulation of the apparatus in these experiments, and the agreement of the three experiments following each other successively is, to say the least, striking.

GROUP II. CASE K.

DESCRIPTION OF THE CASE.

Male; born June, 1863; widower; undertaker; came under observation August 19, 1908.

Family history.—No family history of diabetes. Father died of cholera morbus at 69, and one sister of heart trouble. Wife died 3 weeks after confinement. One sister has "arrested" pulmonary tuberculosis. Mother, two brothers, and one sister well.

Past history.—Healthy child. Pleurisy on left side, with effusion, in 1894. Measles, mumps, whooping cough, and rheumatic pains, without fever, in the left shoulder in 1897.

Present illness.—Onset November, 1907, with polydipsia, polyuria, polyphagia, and weakness. No nausea or vomiting. Bowels moved three to four times daily. No headache. Cough, but no sputum.

Physical examination.—Height, 180 centimeters. Greatest weight, 77.1 kilograms (dressed); November, 1907, 74.9 kilograms (dressed); August, 1908, 62.7 kilograms. (Weight of clothes, 3.8 kilograms.) Healthy-looking man. Pupils equal and react. Teeth partially false. A mass of varices sufficient to make a tumor inside of the left cheek. Heart normal, pulse 96, blood-pressure 100 millimeters (Riva Rocci), lungs normal, abdomen, nothing abnormal felt, knee jerks present, no edema.

General history of the case.—The diet consisted recently of 10 slices of gluten bread daily, in addition to other articles of food.

While under observation, the patient was never troubled with a large quantity of urine, nor did he excrete much sugar, although seldom sugar-free. The sugar disappeared within 2 days after his entrance to the New England Deaconess Hospital. The general health was excellent throughout. Albumen was absent from the urine throughout, save on a few occasions, when only a trace was present. Diacetic acid was never distinctly positive. The general history of the case is shown by the chart (table 138).

TABLE 138.—*Clinical chart—Case K.*

Date.	Experiment No.	Volume of urine.	Specific gravity.	Diacetic acid.	Nitrogen.	Sugar. By Citron.	Sugar. By rotation.	Diet. Carbohydrate.	Diet. Protein.	Diet. Nitrogen.	Diet. Alcohol.	Carbohydrate-balance.	NaHCO$_3$.	Naked body-weight.
1908.		*c. c.*			*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*
Aug. 18-19	......	....	1037	0	....	..	[5]4.2	....	..	..	..	....	..	58.6
Aug. 23-24	......	2125	1025	0	....	..	72	120	..	..	..	+50	0	60.1
Aug. 30-31	......	2000	1031	0	....	..	40	85	..	..	..	+45	0	61.3
Sept. 23-24	......	1500	1026	0	....	..	6	60	..	..	..	+55	0	61.0
Oct. 22-23	......	....	1029	0	....	..	[5]1.4	(?)	..	..	..	....	0	63.1
Oct. 27-28[1]	......	2000	1031	0	24.5	..	32	(?)	..	..	..	....	0	....
Nov. 5-6	......	....	1032	0	....	..	[5]2.4	(?)	..	..	..	....	0	....
Nov. 13-14	......	....	1033	0	....	..	[5]3	(?)	..	..	..	....	0	....
Nov. 20-21	......	1500	....	0	....	..	27	(?)	..	..	..	....	0	63.2
Nov. 26-27	......	....	1033	....	....	..	[5]0.8	15	..	..	..	....	0	....
Dec. 10-11	......	1200	1027	v.sl. +	....	0	....	15	..	..	..	....	0	....
Dec. 30-31	......	....	1028	0	....	0	....	15	..	..	..	....	0	....
1909.														
Feb. 10-11	......	....	1023	0	....	..	[5]0.2	(?)	..	..	..	....	0	....
Feb. 12-13	......	....	1035	0	....	..	[5]0.8	(?)	..	..	..	....	0	63.8
May 10-11	......	1113	....	....	18.1	15	....	....	..	..	..	....	0	....
July 19-20	......	2000	1035	0	....	..	68	(?)	..	..	..	....	0	....
Aug. 9-10	......	....	1040	+	....	..	[5]4.2	(?)	..	..	..	....	0	....
Aug. 11-12	......	1500	1037	0	....	..	75	(?)	..	..	..	....	0	....
Aug. 13-14	......	1530	1031	0	....	..	58	(?)	..	..	..	....	0	....
Aug. 14-15	......	....	....	....	....	..	[5]4	16	90	14	25	....	0	57.4
Aug. 15-16[2]	......	1050	1025	sl. +	....	..	21	16	25	4	25	− 5	0	57.6
Aug. 16-17[2]	......	1680	1015	0	....	..	8	16	25	4	25	+10	0	58.1
Aug. 17-18[2]	......	1200	1021	0	....	0	0	16	25	4	25	+15	0	58.6
Aug. 18-19[3]	......	1680	1012	0	....	0	....	16	45	7	25	+15	0	58.1
Aug. 19-20[3]	......	900	1021	sl. +	....	0	[5]0.8	16	45	7	25	+ (?)	0	58.8
Aug. 20-21[4]	......	1440	1020	0	....		[5]0.8	16	50	8	25	+ (?)	0	59.0
Aug. 21-22	**K 2**	**1688**	**1013**	**0**	....	..	[5]**0.2**	**16**	**50**	**8**	**25**	+ (?)	**0**	**58.9**
Aug. 22-23	......	....	....	....	....	..	....	16	50	8	25	+ (?)	0	59.7

[1] Eggs, bacon, celery; meat, spinach; 500 c. c. cream.
[2] Vegetable day, 250 c. c. cream, 250 c. c. wine and yolks 4 eggs.
[3] The same as August 15-16, and 90 grams meat.
[4] 90 grams meat, 4 eggs, 250 c. c. cream, vegetables.
[5] Per cent.

EXPERIMENTS WITH CASE K.

One metabolism experiment and one respiration experiment were made with this subject, some 3 months apart, and both without food. The vital statistics were as follows:

Date of birth, June, 1863; height, 180 centimeters; range of naked body-weight, 59.1 to 60.6 kilograms.

METABOLISM EXPERIMENT No. K 1.

Date, May 11, 1909. Naked body-weight, 60.6 kilograms.

The subject came to the laboratory in the morning without breakfast and entered the chair calorimeter at 8^h 54^m a. m. The experiment began at 9^h 38^m a. m. and continued for four 1-hour periods, ending at 1^h 38^m p. m. No water was consumed throughout this experiment. The pulse-rate was obtained by means of the stethoscope, the respiration-rate and body-movements with the pneumograph, and the rectal temperature by means of the electrical-resistance thermometer. The individual records of the pulse-rate varied with this subject from 64 to 88, and the respiration-rate from 15 to 19.

The quietest period was during the first hour, and the activity gradually increased with each successive period inside the chamber, although he was in general very quiet, the movements being due in large part to telephoning and urinating.

Records of the metabolism and of the average pulse- and respiration-rates are given in table 139. The carbon-dioxide elimination remained almost unchanged throughout the whole experiment. The oxygen absorption for the last two periods was not calculated, although the results give the sum total for the last two periods. Similarly, in the computation of the respiratory quotient, the average value for carbon dioxide is taken for comparison with the average value for oxygen. An increased pulse-rate and relatively high metabolism are apparent in the first period, notwithstanding the fact that the pneumograph record indicated the least external muscular activity in the period. This is in full accord with our experience with many other subjects, especially during an initial experiment, as we usually find that there is a stimulated muscular tonus throughout the first period of an experiment, which may result in a somewhat increased metabolism. The statistics of the urine are given in table 140.

TABLE 139.—*Measurements of metabolism—Metabolism experiment No. K 1.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.					
May 11, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
9^h 38^m a.m. to 10^h 38^m a.m.	22.3	21.2	189	247	43.8	0.76	85	82	17
10 38 a.m. 11 38 a.m.	21.5	19.7	182	230	38.6	.80	82	73	17
11 38 a.m. 12 38 p.m.	22.0	43.5	187	254	35.1	.75	72	69	18
12 38 p.m. 1 38 p.m.	22.7		193		34.6		79	77	18
Total 4 hours[1].....	88.5	84.4	188	246	152.1	0.76	[2]318	75	17.5

[1] Carbon dioxide eliminated per kilogram per minute, 3.10 c. c.; oxygen absorbed per kilogram per minute, 4.06 c. c.; heat eliminated per kilogram per hour, 1.31 calories.

[2] Rectal body-temperature at beginning, 37.14° C.; at end, 36.93° C. Heat production for total 4 hours, 307 calories.

TABLE 140.—*Statistics of urine—Metabolism experiment No. K 1.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
May 10–11, 1909.	c. c.		grams.	grams.	
$7^h 00^m$ a.m. to $7^h 00^m$ p.m.	243	1.033	4.57	3.4	....
7 00 p.m. 7 00 a.m.	870	1.024	13.57	11.3	....
7 00 a.m. 9 40 a.m.	[1]	.....	1.26	.4	0.32
9 40 a.m. 11 40 a.m.	62	1.025	1.11	.4	.36
11 40 a.m. 1 40 p.m.	88	1.022	1.38	.4	.29

[1] Bottle broken—weight of urine before dilution unknown.

RESPIRATION EXPERIMENT NO. K 2.

Date, August 21, 1909. Naked body-weight, 59.1 kilograms.

Subsequent to the metabolism experiment here reported, this patient was placed about the middle of August in a local hospital and was kept on a practically controlled diet with a relatively low intake of nitrogen, *i. e.,* about 8 grams a day. The carbohydrates in the food were also extraordinarily low, only about 16 grams being given. The subject was at this time practically sugar-free. At this season of the year it was impracticable to conduct experiments with the respiration calorimeter, but by means of the respiration apparatus it was possible to determine the gaseous exchange.

The subject came to the laboratory at $7^h 30^m$ a. m., August 21, without having taken any food, and immediately lay down on the couch. Since this was the subject's first experience with the respiration apparatus and he was entirely unfamiliar with it, an unusual amount of preliminary experimenting was necessary in order to avoid a leakage of air and to adjust him to the apparatus. It was furthermore impracticable to cover the mouth with surgeon's plaster and ensure a tight closure as the subject had a short and stiff mustache.

The experiment included five periods, lasting from 10 to 13.5 minutes each. The subject took every precaution not to open his mouth, lay perfectly quiet, and cooperated in every way with the experiment. The nosepieces caused him no discomfort, but he reported that it was very unusual for him to lie quiet for such a long time. No urine was passed during the experiment or soon afterwards. The subject left the hospital a few days after this experiment was made.

A summary of the respiratory exchange during the experiment is given in table 141. The records for the pulse and respiration, which are also included in the table, are the averages of a number of observations during each period. The slightly larger carbon-dioxide output shown in the first period is commonly experienced in experiments of this kind, and indicates a possible abnormal respiration due to the novelty of the situation. Consequently in computing the averages for this experiment only the last four periods were taken.

TABLE 141.—*Results of respiration experiment No. K 2.*

Date and time.	Duration.		Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
August 21, 1909.	*m.*	*s.*	*c. c.*	*c. c.*			
8h 40m a.m.	10	30	187	247	0.76	76	15
9 01 a.m.	10	..	168	239	.70	75	16
9 19 a.m.	13	30	166	234	.71	75	16
9 41 a.m.	10	10	170	245	.69	75	18
9 59 a.m.	10	..	167	237	.70	75	13
Average [1]			168	239	0.70	75	16

[1] First period not included in average. Carbon dioxide eliminated per kilogram per minute, 2.85 c. c.; oxygen absorbed per kilogram per minute, 4.05 c. c.

COMPARISON OF THE EXPERIMENTS WITH CASE K.

In comparing the results of the respiration experiment with this subject with the metabolism experiment made inside the respiration chamber, it is important to take into consideration the difference in body-position and muscular activity. In the respiration experiment the subject was lying quietly, with minimum muscular movement, and we find the total metabolism as measured by the carbon-dioxide elimination and oxygen absorption somewhat lower than in the earlier experiment. There is a marked decrease in the carbon-dioxide production per minute, amounting to some 20 c. c., while there is but a small diminution in the oxygen consumption.

The most striking feature is the noticeable decrease in the respiratory quotient, which in the metabolism experiment in May was 0.76 and in the respiration experiment in August was 0.70, again indicating a decrease of carbohydrates in the body. The patient was practically sugar-free and the fact that he was less muscularly active is the only interpretation of this low respiratory quotient, as indicating that there was a low storage of glycogen to be drawn upon during the fasting period. The average pulse-rate remained essentially the same in both experiments, while the respiration rate was somewhat lower in the respiration experiment. Taking the oxygen as an index of the total energy transformations, we see that there is practically very little difference in the two experiments. The decreased carbon-dioxide elimination is accounted for by the difference in the kind of material katabolized, a larger proportion of body-fat being substituted in the second experiment for the carbohydrate katabolized in the first experiment.

GROUP II. CASE L.

DESCRIPTION OF THE CASE.

Male; born October 18, 1886; single; student; came under observation December 15, 1908.

Family history.—No family history of diabetes. A brother and sister died at birth. Father, mother, three brothers, and two sisters well.

Past history.—Measles, mumps, whooping cough, and chicken-pox. Appendicitis, with operation, in 1900.

Present illness.—In July, 1908, polydipsia, polyuria, and weariness appeared. The diagnosis of diabetes was not made until December 9, 1908. Except for weariness, the patient appeared in good health. From July, 1908, to December, 1908, the patient took considerable exercise, but this was reduced as soon as he came under treatment.

Physical examination.—Greatest weight, stripped, summer, 1908, 79 kilograms; December 11, 1908, stripped, 64.7 kilograms, and December 15, 1908, 67.2 kilograms, stripped. Height, 6 feet (183 centimeters). Healthy-looking young man with red cheeks. Pupils equal and react, knee jerks present, lungs normal, heart normal, pulse 56, blood-pressure 110 mm. (Riva Rocci). Abdomen, nothing abnormal found.

General history and treatment of case.—The history of the case is given in the chart herewith (table 142).

The patient reacted quickly to the change of diet, the percentage of sugar falling in 24 hours from 6.8 per cent to 1.2 per cent. Jaundice developed almost immediately upon restriction of carbohydrates with the increase of fat in the diet, but persisted for only about 1 week. The jaundice was extreme and appeared like a typical gastro-duodenal catarrh. Even when he had jaundice, the subject appeared in perfect health and spirits and always reiterated that he felt extremely well. He bore the diet with unusual comfort, and after the first few days consumed a good quantity of fatty food.

Although the volume of urine was reported as 6000 c. c. upon December 13–14, it never approached this quantity again. Albumen was absent except during the attack of jaundice, December 18–24. The reaction of the urine was acid throughout, except for 1 day. Sodium bicarbonate was at no time given. Diacetic acid was never present.

Despite the large quantity of urine and sugar which the patient had at the onset, the case must be considered a mild one, because diacetic acid was absent throughout, and because a positive carbohydrate-balance of 50 grams was soon obtained. Undoubtedly the patient would have become sugar-free more promptly if a vegetable day or starvation day had been earlier instituted. This is evident by the quick response to a vegetable day 10 months later, when sugar had temporarily reappeared.

TABLE 142.—*Clinical chart—Case L.*

Date.	Experiment No.	Volume of urine.	Specific gravity.	Diacetic acid.	Nitrogen.	Sugar. By Citron.	Sugar. By rotation.	Diet. Carbohydrate.	Diet. Protein.	Diet. Nitrogen.	Diet. Fat.	Diet. Alcohol.	Carbohydrate balance.	Naked body-weight.
		c. c.			*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*
1908.														
Dec. 13-14	......	6000	....	..	....	..	...	...	...	...	...	..	....	....
Dec. 14-15	......	....	1037	0	....	..	[1]6.8	...	...	...	...	..	....	67.3
Dec. 17-18[2]	......	1920	1021	0	....	..	23	(?)	...	...	...	..	(?)	....
Dec. 19-20[2]	......	2070	1028	0	....	..	70	(?)	...	...	...	..	(?)	....
Dec. 21-22[2]	......	1690	1025	0	....	..	44	(?)	...	...	...	..	(?)	....
Dec. 23-24[3]	......	2250	1031	0	....	..	77	(?)	...	...	...	..	(?)	....
Dec. 20-21[4]	......	3125	1033	0	....	..	163	150	135	22	240	13	—15	....
Dec. 28-29	......	2310	1036	0	....	..	106	110	130	21	220	13	+ 5	66.2
Dec. 30-31	......	2125	1031	0	....	..	64	85	135	22	220	18	+20	64.2
1909.														
Dec. 31-Jan. 1[5]	......	1020	1023	..	8.4?	21	...	...	...	...	...	..	....	....
Jan. 1-2	**L 1**	**1700**	....	..	**19.6**	**16**	...	**56**	...	...	...	..	**+40**	....
Jan. 2-3	......	1860	1028	0	....	..	26	80	135	22	220	13	+55	....
Jan. 4-5	......	1500	1029	0	....	..	6	50	125	20	210	19	+45	....
Jan. 5-6	......	1625	1028	0	....	..	3	60	130	21	210	19	+55	....
Jan. 7-8	......	1560	1030	0	....	..	5	35	105	17	200	19	+30	....
Jan. 8-9	......	1380	....	0	20.5	0	...	35	105	17	200	19	....	....
Jan. 9-10	**L 2**	**1350**	....	**0**	**19.3**	+	...	**25**	**75**	**12**	**140**	**15**	....	....
Jan. 10-11	......	1500	....	0	....	..	5	35	105	17	200	19	+30	66.2
Jan. 13-14	......	1625	1029	0	....	..	3	35	105	17	200	19	+30	....
Jan. 17-18	......	1565	1022	0	....	0	...	35	105	17	200	19	+35	....
Jan. 19-20	......	1530	1030	0	....	0	...	35	105	17	200	19	+35	....
Jan. 22-23	......	1375	....	0	....	0	...	35	105	17	200	19	+35	....
Jan. 25-26	......	1280	....	0	20.5	4	...	35	105	17	200	19	+30	....
Jan. 29-30	......	1280	....	..	....	4	...	35	105	17	200	19	+30	....
Feb. 1-2	......	1250	1035	0	....	0	...	40	...	...	...	..	+40	62.2
Feb. 5-6	......	1375	1025	0	....	0	...	40	...	...	...	..	+40	62.6
Feb. 8-9	......	1375	....	0	....	3	...	50	...	...	...	..	+45	....
Feb. 10-11	......	1250	1017	0	....	..	0	50	...	...	...	..	+50	....
Feb. 15-16	......	1375	1028	0	....	(?)	0	50	...	...	...	..	+50	....
Feb. 26-27	......	1563	1023	0	....	0	...	39	...	...	...	..	+40	63.5
Mar. 5-6[6]	......	1375	1030	0	....	0	...	45	...	...	...	..	+45	64.9
Mar. 16-17[7]	......	1500	1025	0	....	0	...	50	100	...	...	..	+50	65.6
Mar. 25-26	......	1320	....	..	12	11	...	..	...	...	...	..	....	....
Oct. 11-12	......	....	1028	0	....	+	[1]4.4	80	...	...	...	..	....	68.9
Oct. 13-14	......	1500	1034	0	....	..	27	30	105	17	200	..	0	69.2
Oct. 14-15[8]	......	1565	1023	0	....	0	...	10	...	...	...	..	+10	70.2
Oct. 16-17	......	1500	1026	0	....	0	...	13	66	...	...	..	+15	69.9
Oct. 21-22	......	1500	1031	0	....	..	42	(?)	...	...	...	..	....	....
Oct. 25-26	......	1250	1030	0	....	..	5	(?)	...	...	...	..	....	69.9
Oct. 26-27[8]	......	1375	1028	0	....	0	...	10	...	...	...	..	+10	....
Oct. 28-29	......	1500	1026	0	....	0	...	10	100	...	200	..	+10	69.7
Nov. 2-3	......	1750	1031	0	....	0	...	10	100	...	200	..	+10	69.3
Nov. 10-11	......	....	....	..	....	0	...	12	...	...	...	..	....	69.3
Nov. 23-24	......	1750	1035	0	....	0	...	15	100	...	200	..	+15	....
1910.														
Feb. 23-24	......	1500	1025	Sl. +	....	0	...	..	...	...	...	..	....	68.1

[1] Per cent.
[2] Bile in urine.
[3] Bile sl. + in urine.
[4] No bile in urine.
[5] For 12 hrs.
[6] Nitrogen 20 grams.
[7] 7 grams sugar first 12 hrs.—none in second.
[8] Vegetable day.

EXPERIMENTS WITH CASE L.

Five metabolism experiments were carried out with this subject, in all cases after a 12-hours' fast and without breakfast. No respiration experiments were made with him. The vital statistics were as follows:

Date of birth, October 18, 1886; height, 183 centimeters; range of naked body-weight, 63 to 65.5 kilograms.

METABOLISM EXPERIMENT No. L 1.

Date, January 1, 1909. Naked body-weight, 64.6 kilograms.

The subject came to the laboratory without breakfast and entered the chair calorimeter at $8^h\ 05^m$ a. m. The experiment proper began at $9^h\ 52^m$ a. m. and continued for five 1-hour periods, ending at $2^h\ 52^m$ p. m. No water was consumed. Aside from sitting still so long, the subject reported that he was very comfortable and did not feel particularly hungry. The pulse-rate was taken by means of the stethoscope and ranged from 66 to 86. The body-temperature was measured with the electrical-resistance thermometer. Measurements were also taken sublingually by the subject with clinical thermometers as a possible control upon the measurements by the rectal thermometer, and to give evidence regarding the uniformity in temperature changes in the body at different points. With this particular subject the agreement between the measurements with the clinical thermometer and the rectal thermometer was very satisfactory. No pneumograph curve was made in this experiment and the respiration-rate was not recorded. The records of the physical observer show that the subject was telephoned to once during each period, but for the most part he sat very quietly reading.

TABLE 143.—*Measurements of metabolism—Metabolism experiment No. L 1.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.				
January 1, 1909.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
$9^h 52^m$ a.m. to $10^h 52^m$ a.m.	28.5	26.4	242	308	28.0	0.78	88	79
10 52 a.m. 11 52 a.m.	26.6	24.8	226	289	28.1	.78	86	84
11 52 a.m. 12 52 p.m.	27.6	25.1	234	293	29.1	.80	83	81
12 52 p.m. 1 52 p.m.	25.7	25.7	218	300	28.0	.73	84	77
1 52 p.m. 2 52 p.m.	26.1	24.0	221	280	28.5	.79	80	72
Total 5 hours [1]	134.5	126.0	228	294	141.7	....	[2]421	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.53 c. c.; oxygen absorbed per kilogram per minute, 4.55 c. c.; heat eliminated per kilogram per hour, 1.30 calories.
[2] Rectal body-temperature at beginning, 37.15° C.; at end, 37.22° C. Heat production for total 5 hours, 427 calories.

The results of the metabolism are given in table 143, and the urine data in table 144. The first period, as is frequently the case with new subjects, is characterized by a large carbon-dioxide excretion which subsequently decreases some-

what. The last four periods show a general regularity in the metabolism as a whole. The respiration-rate was not recorded in this experiment. The pulse-rate decreased somewhat as the experiment progressed. From the respiratory quotient one would assume that this subject had a high glycogen storage and drew upon this regularly throughout the whole 5 hours of the experiment. The abnormally low quotient and pulse-rate are probably without particular significance, and only the average respiratory quotient for the whole experiment can be considered.

TABLE 144.—*Statistics of urine—Metabolism experiment No. L 1.*

Date and period.	Quantity.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
January 1–2, 1909.	*c. c.*		*grams.*	*grams.*	
$7^h 00^m$ a.m. to $9^h 52^m$ a.m.	[1]167	....	2.05	1.3	0.63
9 52 a.m. 11 52 a.m.	81	1.030	1.07	.3	.28
11 52 a.m. 1 52 p.m.	[1]56	....	.92	.2	.22
1 52 p.m. 2 52 p.m.	[1]22	....	.41	.1	.24
2 52 p.m. 7 00 a.m.	1380	....	15.11	14.1	....

[1] Grams.

METABOLISM EXPERIMENT NO. L 2.

Date, January 9, 1909. Naked body-weight, 64 kilograms.

The subject came to the laboratory in the morning without breakfast and entered the chair calorimeter at $8^h 05^m$ a. m. The experiment began at $8^h 47^m$ a. m. and continued for six 1-hour periods, ending at $2^h 47^m$ p. m. The subject drank no water and used the telephone at the beginning of each period. The stethoscope was used to obtain the pulse-rate, which ranged from 61 to 77, and

TABLE 145.—*Measurements of metabolism—Metabolism experiment No. L 2.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.				
January 9, 1909.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
$8^h 47^m$ a.m. to $9^h 47^m$ a.m. ..	26.5	26.6	225	310	26.7	0.73	88	73
9 47 a.m. 10 47 a.m. ..	26.1	....	221	...	24.5	....	88	71
10 47 a.m. 11 47 a.m. ..	26.3	25.5	223	298	25.1	.75	84	63
11 47 a.m. 12 47 p.m. ..	24.8	24.0	210	280	25.3	.75	87	63
12 47 p.m. 1 47 p.m. ..	24.7	24.6	210	287	25.0	.73	85	63
1 47 p.m. 2 47 p.m. ..	26.7	24.9	227	291	25.6	.78	85	71
Total 6 hours [1]	155.1	125.6	219	[2]293	152.2	....	[3]517	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.42 c. c.; oxygen absorbed per kilogram per minute, 4.58 c. c.; heat eliminated per kilogram per hour, 1.34 calories.
[2] Does not include period from $9^h 47^m$ a. m. to $10^h 47^m$ a. m.
[3] Rectal body-temperature at beginning, 37.07° C.; at end, 37.07° C. Heat production for total 6 hours, 517 calories.

the body-temperatures were recorded by the rectal thermometer; clinical thermometers were also used as a control upon the measurements with the rectal thermometer. On coming out of the chamber the subject reported that he experienced even less discomfort than in the previous experiment.

The metabolism is given in table 145, and the statistics for the urine in table 146. The noticeable fall in the carbon-dioxide production in the first experiment with this subject does not appear here, and the measurements of the oxygen consumption were lost in the second period. The respiration-rate was not determined during this experiment, but records of the pulse-rate varied considerably for a subject at rest. The low respiratory quotient during the fifth period, and the somewhat higher one during the sixth are probably due to a compensation and are without significance. The average value of 0.75 is somewhat lower than in the previous experiment. In general this 6-hour experiment indicates that the metabolism of the subject 12 hours after the last meal is relatively constant from hour to hour.

TABLE 146.—*Statistics of urine—Metabolism experiment No. L 2.*

Date and period.	Quantity.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
January 9–10, 1909.	*c. c.*		*grams.*	*grams.*	
$7^h 00^m$ a.m. to $8^h 50^m$ a.m.	104	1.025	1.27	0.6	0.47
8 50 a.m. 10 50 a.m.	121	1.025	1.37	.4	.29
10 50 a.m. 12 50 p.m.	[1] 105	....	1.19	.3	.25
12 50 p.m. 2 50 p.m.	[1] 66	....	.89	.1	.11
?4 00 p.m. 7 00 a.m.	960	....	14.58	...	....

[1] Grams.

METABOLISM EXPERIMENT No. L 3.

Date, January 26, 1909. Naked body-weight, 63 kilograms.

The subject entered the chair calorimeter for this experiment at $7^h 50^m$ a. m., without breakfast. The experiment began at $8^h 51^m$ a. m. and continued for six 1-hour periods, ending at $2^h 51^m$ p. m. No water was consumed. The pulse-rate was obtained by means of the stethoscope and ranged from 61 to 82, but the respiration-rate and the pneumograph curve were not obtained in this experiment. The body-temperature was measured by the rectal thermometer.

The results of the metabolism are reported in table 147, and the urine statistics in table 148. All six periods are characterized by having unusually regular and uniform metabolism as measured by the oxygen consumption and the carbon-dioxide production. The heat-elimination decreased noticeably as the experiment continued. The values for the respiratory quotient varied considerably from period to period, but the average of the whole six periods indicates a value of 0.75. The pulse-rate also noticeably fell off as the experiment progressed.

TABLE 147.—*Measurements of metabolism—Metabolism experiment No. L 3.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.
January 26, 1909.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
8h 51m a.m. to 9h 51m a.m. .	26.6	25.5	226	298	28.6	0.75	91	80
9 51 a.m. 10 51 a.m. .	24.7	23.1	210	270	28.4	.78	88	75
10 51 a.m. 11 51 a.m. .	25.6	26.0	217	303	29.3	.71	87	71
11 51 a.m. 12 51 p.m. .	25.2	25.0	214	292	27.1	.73	82	68
12 51 p.m. 1 51 p.m. .	25.6	23.4	217	273	27.5	.79	80	65
1 51 p.m. 2 51 p.m. .	26.7	27.0	227	315	27.0	.72	79	66
Total 6 hours[1]	154.4	150.0	218	292	167.9	0.75	[2]507	. .

[1] Carbon dioxide eliminated per kilogram per minute, 3.46 c. c.; oxygen absorbed per kilogram per minute, 4.64 c. c.; heat eliminated per kilogram per hour, 1.35 calories.
[2] Rectal body temperature at beginning, 36.80° C.; at end, 36.93° C. Heat production for total 6 hours, 514 calories.

TABLE 148.—*Statistics of urine—Metabolism experiment No. L 3.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
January 26, 1909.	*c. c.*		*grams.*	*grams.*	
7h 00m a.m. to 8h 55m a.m.......	76	1.027	1.20	0.3	0.25
8 55 a.m. 10 55 a.m.......	89	1.026	1.27	.3	.24
10 55 a.m. 12 56 p.m.......	79	1.026	1.13	.3	.27
12 56 p.m. 2 50 p.m.......	57	1.027	.85	.2	.24

METABOLISM EXPERIMENT NO. L 4.

Date, February 11, 1909. Naked body-weight, 63 kilograms.

The bed calorimeter was used for this experiment. The subject came to the laboratory without breakfast and entered the calorimeter chamber at $8^h\ 04^m$ a. m. The experiment began at $9^h\ 22^m$ a. m. and continued for six 1-hour periods, ending at $3^h\ 22^m$ p. m. At $11^h\ 58^m$ a. m. the subject drank 199 c. c. of water. The pulse- and respiration-rates were obtained by means of the stethoscope and pneumograph and ranged from 54 to 58 and from 17 to 22, respectively. The body-temperature was measured by means of the electrical-resistance thermometer. In the experiment the subject lay on the mattress without a coat and covered with a blanket up to the waist.

The muscular activity during this experiment was greatest from $11^h\ 22^m$ a. m. to $11^h\ 52^m$ a. m.; during most of this time he was unsuccessfully attempting to urinate. During the rest of the experiment he was quiet the greater part of the time. The subject reported that he was asleep or dozing most of the first period, while in the last part of the experiment he was more awake, especially at the end of the fifth period. Part of the time he lay on his back and at another time on the left side, so that he was as a rule perfectly comfortable and quiet.

The data for the metabolism are given in table 149, and the urine data in table 150. The carbon-dioxide production was relatively constant, except for the fifth period, when it rose 3 grams. This is accompanied by a large increase in the oxygen consumption and consequently a marked lowering of the respiratory quotient. On the other hand, the highest heat-elimination was reported in the last period. The averages for both pulse- and respiration-rates include but two or three observations in each period, as the pneumograph and stethoscope were not adjusted in a particularly satisfactory manner, and records could only be obtained intermittently.

TABLE 149.—*Measurements of metabolism—Metabolism experiment No. L 4.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
February 11, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
9h 22m a.m. to 10h 22m a.m.	23.9	22.0	203	257	26.7	0.79	73	57	19
10 22 a.m. 11 22 a.m.	25.5	23.4	216	273	29.9	.79	81	55	20
11 22 a.m. 12 22 p.m.	25.1	21.0	213	245	22.8	.87	86	..	19
12 22 p.m. 1 22 p.m.	25.2	22.4	214	261	22.3	.82	79	56	..
1 22 p.m. 2 22 p.m.	28.2	29.4	239	343	33.1	.70	77	56	19
2 22 p.m. 3 22 p.m.	25.8	24.6	219	287	32.9	.76	88	57	20
Total 6 hours[1]	153.7	142.8	217	278	167.7	....	[2]484	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.44 c. c.; oxygen absorbed per kilogram per minute, 4.41 c. c.; heat eliminated per kilogram per hour, 1.29 calories.
[2] Rectal body-temperature at beginning, 37.71° C.; at end, 37.65° C. Heat production for total 6 hours, 481 calories.

TABLE 150.—*Statistics of urine—Metabolism experiment No. L 4.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
February 11, 1909.	*c. c.*		*grams.*	*grams.*	
7h 00m a.m. to 1h 25m p.m.	580	1.016	4.16	0.5	0.12
1 25 p.m. 3 30 p.m.	95	1.019	.98	.2	.20

METABOLISM EXPERIMENT No. L 5.

Date, March 27, 1909. Naked body-weight, 65.5 kilograms.

The subject came to the laboratory without breakfast and entered the chair calorimeter at 8h 02m a. m. The experiment began at 9h 07m a. m. and continued for four 1-hour periods, ending at 1h 07m p. m. No water was consumed during the experiment. The stethoscope and pneumograph were used to obtain the pulse- and respiration-rates which ranged from 62 to 80 and from 16 to 21, respectively. The rectal thermometer was used to measure the body-temperature.

The muscular activity was greatest in the first period and the least during the third period.

The results of the metabolism are given in table 151, and the urine data in table 152. There was a noticeable decrease in the carbon-dioxide production after the first period, and the oxygen determination was also quite irregular. It is evident, therefore, that in this experiment we must take the average oxygen determination for the whole experiment as a true value rather than the values for the periods, and the same is obviously true with regard to the respiratory quotient. The pulse-rate fell off perceptibly as the experiment progressed. The heat-elimination was the largest in the first period and followed in general the decrease in the carbon-dioxide production and oxygen absorption. The average of the pulse- and respiration-rates are the results of a number of observations during each period.

TABLE 151.—*Measurements of metabolism—Metabolism experiment No. L 5.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed					
March 27, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$9^h 07^m$ a.m. to $10^h 07^m$ a.m.	27.8	28.1	236	328	27.5	0.72	96	76	18
10 07 a.m. 11 07 a.m.	25.9	21.7	220	253	27.9	.87	88	70	20
11 07 a.m. 12 07 p.m.	25.7	24.9	218	291	27.8	.75	88	67	20
12 07 p.m. 1 07 p.m.	26.1	23.1	221	270	28.1	.82	87	65	20
Total 4 hours[1]	105.5	97.8	224	285	111.3	....	[2]359	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.42 c. c.; oxygen absorbed per kilogram per minute, 4.35 c. c.; heat eliminated per kilogram per hour, 1.37 calories.
[2] Rectal body-temperature at beginning, 37.09° C.; at end, 37.13° C. Heat production for total 4 hours, 363 calories.

TABLE 152.—*Statistics of urine—Metabolism experiment No. L 5.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.	D : N.
March 26–27, 1909.	*c. c.*		*grams.*	*grams.*	
$7^h 00^m$ a.m. to $7^h 00^m$ p.m.	600	....	5.49	7.7	....
7 00 p.m. 7 00 a.m.	720	....	6.54	2.8	....
7 00 a.m. 9 07 a.m.	65	1.025	1.29	.2	0.16
9 07 a.m. 11 07 a.m.	127	1.024	1.73	.4	.23
11 07 a.m. 1 07 p.m.	84	1.024	1.18	.2	.17

COMPARISON OF THE EXPERIMENTS WITH CASE L.

As will be seen from an examination of the chart, the progress of the disease in this subject was such as to make a comparison of these different experiments desirable. It should be borne in mind, also, that during the first experiment the subject was just recovering from a marked jaundice. An examination of the figures given in table 153, in which a comparison of all the experiments is made, shows that the carbon-dioxide excretion was relatively constant for all experiments and did not materially decrease in the experiment with the bed calorim-

eter, where the muscular activity must have been somewhat less than in the other experiments. The oxygen consumption, however, was somewhat less in the bed calorimeter than in any other experiment, although not noticeably so. The respiratory quotient remained relatively constant throughout all five experiments, while the heat-elimination was somewhat lower in the bed calorimeter than in the other experiments. There was a very marked decrease in the pulse-rate while the subject was inside the bed calorimeter.

In general, therefore, it is seen that these experiments substantiate very clearly the constancy of metabolism in this subject, and, indeed, during the period in which these experiments extended from January 1 to March 27, there was no material alteration in the metabolism of this subject. The respiratory quotients indicate a fairly liberal supply of glycogen that could be drawn upon when food was not given. This is probably of special significance, inasmuch as the diet throughout the whole of these tests contained a relatively small amount of carbohydrates, *i. e.*, 35 to 50 grams, and notwithstanding this very low carbohydrate intake, the store of glycogen was fairly large.

TABLE 153.—*Comparison of metabolism experiments with Case L.*

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Respiratory quotient.	Heat eliminated per hour.	Heat produced per hour.	Average pulse-rate per minute.	Average respiration per minute.
	1909.	*kilos.*	*hrs.*	*c. c.*	*c. c.*		*cals.*	*cals.*		
L 1	Jan. 1.......	64.6	....	228	294	0.78	84	85	79	....
L 2	Jan. 9.......	64.0	....	219	293	.75	86	86	67	....
L 3	Jan. 26.......	63.0	....	218	292	.75	85	86	71	....
L 4	Feb. 11[1]......	63.0	....	217	278	.78	81	80	56	19.5
L 5	Mar. 27.......	65.5	....	224	285	.79	90	91	70	19.5

[1] Bed calorimeter.

GROUP III. CASE M.

DESCRIPTION OF THE CASE.

Male; born January 23, 1853; married; dentist; came under observation January 6, 1908.

Family history.—Father died of pulmonary tuberculosis at 56 and mother of typhoid fever at 67; one sister died of apoplexy, and possibly had diabetes mellitus; one sister and two brothers died of typhoid fever; one brother probably has diabetes mellitus; one sister is 77 and well; five healthy children; one child died of pneumonia at 18 years of age.

Past history.—Not a vigorous child. Diphtheria at 15, typhoid fever at 18, considerable indigestion as a boy; at 25 or 26 years of age troubled with gallstones during a period of 4 or 5 years. The patient has been a sugar-eater, especially of maple-sugar and candy since boyhood.

Present illness.—Sugar was detected in 1900 in the urine upon application for life insurance. Since this date the greatest volume of urine observed was July, 1906, when it was 2500 c. c. The largest per cent of sugar did not exceed 2 per cent. Patient has remained in good health from January 6, 1908, up to the present time, except for a moderate attack of inflammation in the region of the gall-bladder during April 3 and 4, 1908. During this period he has taken very little exercise, although working long hours even aside from his professional work.

Physical examination.—Fat man, greatest weight, 86.2 kilograms, stripped; weight January 6, 1908, 84.8 kilograms. Height, 172 centimeters. Pupils equal and react, knee jerks normal, lungs normal. Heart extended 2 centimeters to the left of the mammillary line. Sounds normal. Blood-pressure 120 mm. (Riva Rocci) May 26, 1908, and 115 mm. October 30, 1909. Liver extends 2 fingers' breadth below the costal margin. Spleen not felt.

General history of case.—The history of the case may be seen from the chart (table 154). The volume of urine did not exceed 1820 c. c. from January 7, 1908, until March 5, 1910. The reaction was acid throughout. Albumen was either absent or present in only a very slight trace. Diacetic acid was present

TABLE 154.—*Clinical chart—Case M.*

Date.	Experiment No.	Volume of urine.	Specific gravity.	Diacetic acid.	Nitrogen.	Sugar. By Citron.	Sugar. By rotation.	Diet. Carbohydrate.	Carbohydrate-balance.	$NaHCO_3$.	Naked body-weight.
1908.		c. c.			gms.	gms.	gms.	gms.	gms.	gms.	kilos.
Jan. 6– 7	......	....	1031	0	....	..	[1]	....	...	..	....
Jan. 8– 9	......	1820	1030	0	....	..	55	200	145	0	84.8
Jan. 24–25	......	1380	1036	....	....	..	52	150	...	0	85.2
Feb. 4– 5	......	1400	1029	....	....	..	28	100	80	0	85.3
Feb. 11–12	......	1480	1032	0	....	..	41	50	11	0	....
Feb. 19–20	......	1260	1029	0	....	..	15	60	45	0	....
Mar. 5– 6	......	1120	1023	Sl. +	....	..	7	55	50	0	84.2
Mar. 12–13	......	1180	1037	+	....	..	7	(?)	...	0	....
Mar. 18–19	......	1370	....	Sl. +	....	..	11	(?)	...	..	....
Mar. 23–24	......	1210	....	0	....	..	16	(?)	...	..	[2]84.2
Mar. 28–29	......	1260	1027	Sl. +	....	..	8	(?)	...	..	....
Mar. 30–31	......	....	....	....	....	..	[3]	(?)	...	..	....
Apr. 2– 3	......	1060	....	0	....	0	..	(?)	...	..	....
Apr. 9–10	......	....	....	+	....	0	..	(?)	...	20±	83.5
May 8– 9	......	....	1031	Sl. +	....	..	[4]	(?)	...	..	....
May 22–23	......	1080	1027	Sl. +	14.5	..	3	(?)	...	..	[5]83.9
July 15–16	......	1135	1029	0	....	..	7	(?)	...	..	....
Aug. 10–11	......	....	....	....	....	..	..	....	...	..	81.0
Aug. 13–14	......	900	1028	0	....	0	..	(?)	...	..	....
Sept. 18–19	......	1500	1025	....	....	..	9	(?)	...	..	....
Oct. 30–31	......	970	1026	0	11	+	2	(?)	...	..	....
Nov. 10–11	......	1200	1025	....	....	0	0	(?)	...	..	....
Dec. 28–29	......	900	1026	V. sl. +	....	0	..	(?)	...	..	....
1909.											
Feb. 8– 9	......	1080	1027	0	....	..	4	55	53	..	83.0
Mar. 1– 2	......	1000	1026	0	....	+	4	(?)	...	..	....
Apr. 23–24	......	1060	1029	0	16.4	6	2	(?)	...	..	....
Oct. 28–29	......	840	1029	0	....	..	0	(?)	...	..	81.0
Nov. 26–27	......	915	....	....	15.2	..	..	(?)	...	..	....
1910.											
Mar. 4– 5	......	920	1024	0	....	..	0	....	...	..	....

[1] 3.4 per cent. [2] On Mar. 26, 1908. [3] 0.4 per cent. [4] 0.6 per cent. [5] On May 26, 1908.

only twice and then in a small quantity. The quantity of sugar in the urine decreased from 55 grams on January 9, 1908, to 8 grams on March 29, 1908, and since that time has either been absent or present in a quantity not exceeding 9 grams.

The diet was never accurately controlled, but has varied between 200 grams of carbohydrates at the start to 50 to 100 grams of carbohydrates at the present time. The weight has been nearly maintained and the patient has enjoyed excellent health.

EXPERIMENTS WITH CASE M.

Three metabolism experiments were carried out with this subject, all without breakfast. No respiration experiments were made. The vital statistics were as follows:

Date of birth, January 23, 1853; height, 172 centimeters; range of naked body-weight, 81.4 to 83.1 kilograms.

METABOLISM EXPERIMENT NO. M 1.

Date, February 27, 1909. Naked body-weight, 81.8 kilograms.

The subject arrived at the laboratory in the early morning, without breakfast, and in order to prevent the possible necessity for defecation during the experiment the lower bowel was emptied by means of a warm-water enema. The pneumograph was adjusted about the chest, the stethoscope was also adjusted, and the electrical-resistance thermometer inserted in the rectum. The subject then lay down on the air mattress and was placed in the bed calorimeter at $8^h\ 17^m$ a. m. The experiment proper began at $9^h\ 07^m$ a. m. and continued for three 1-hour periods, ending at $12^h\ 07^m$ p. m. No urine was passed by the subject while inside the chamber, but immediately afterwards he passed 598 grams. No water was consumed and the patient remained drowsy and quiet most of the time.

This was the subject's first experience inside the apparatus, but he did not find it disagreeable, although as he was a large man, the narrow confines of the chamber made it rather difficult for him to move around. The adjustment of the clothing also caused him some annoyance, as it interfered with his reading a paper which he took into the calorimeter. During the experiment the stethoscope connections were not satisfactory and the pulse was therefore taken by the subject himself. Only two records were made, these being 78 and 80, both of these records being taken at $11^h\ 40^m$ a. m.

The muscular activity was materially less in the last period than in the other two, with apparently but little difference between the first two periods. Throughout the whole experiment the subject remained very quiet and the results may therefore be considered to indicate very satisfactorily the resting metabolism of this subject in bed under quiet conditions.

The measurements of the metabolism are given in table 155. An examination of the results given in the table shows that the metabolism as measured by the

carbon-dioxide production, oxygen consumption, and heat-elimination remained essentially the same in the first two periods, but there was a noticeable decrease in all three factors during the last period, and it is reasonable to attribute the decrease to a lessening of muscular activity. The average of the three periods, therefore, gives a fair indication of the metabolism of this subject under the experimental conditions.

TABLE 155.—*Measurements of metabolism—Metabolism experiment No. M 1.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute.		Water vaporized.	Respiratory quotient.	Heat eliminated.	Average respiration-rate.
			Carbon dioxide eliminated.	Oxygen absorbed.				
February 27, 1909.	*grams.*	*grams.*	*c. c.*	*c. c.*	*gms.*		*cals.*	
$9^h 07^m$ a.m. to $10^h 07^m$ a.m. .	25.2	23.2	214	271	22.6	0.79	87	10
10 07 a.m. 11 07 a.m. .	25.7	23.6	218	275	22.8	.79	82	13
11 07 a.m. 12 07 p.m. .	23.5	22.0	199	257	23.5	.78	75	11
Total 3 hours [1]......	74.4	68.8	210	268	68.9	....	[2]244	..

[1] Carbon dioxide eliminated per kilogram per minute, 2.57 c. c.; oxygen absorbed per kilogram per minute, 3.28 c. c.; heat eliminated per kilogram per hour, 0.99 calories.
[2] Heat production for total 3 hours, 241 calories.

METABOLISM EXPERIMENT No. M 2.

Date, April 24, 1909. Naked body-weight, 83.1 kilograms.

Although this subject had not been under a strict hospital diabetic regimen subsequent to the previous experiment, it seemed desirable to make a control experiment with him. Owing to his large size and the narrow confines of the chamber in the bed calorimeter, he preferred that the chair calorimeter should be used for this experiment, and it was consequently so arranged.

The subject came to the laboratory early in the morning and entered the respiration chamber at $8^h 17^m$ a. m., without breakfast. The experiment proper began at $9^h 12^m$ a. m. and continued for four 1-hour periods, ending at $1^h 12^m$ p. m. No urine was passed during the experiment, but the subject drank 128 c. c. of water at $11^h 20^m$ a. m. The pulse- and respiration-rates were obtained by means of the stethoscope and pneumograph, and ranged from 67 to 82 and from 10 to 17, respectively. The rectal body-temperature was measured by means of the electrical-resistance thermometer.

The muscular activity in this experiment differed somewhat from that in the bed calorimeter by virtue of the fact that the subject was sitting in a chair and could read more readily, and consequently there was some slight muscular movement in turning over the leaves of the book or paper. He also used the telephone a number of times. In this experiment the drinking of water called for a certain amount of muscular effort which did not appear in the first experiment, but the subject was not unduly restless inside the chamber. The least muscular activity appears to have been in the period from $10^h 11^m$ a. m. to $11^h 11^m$ a. m.

The results of the metabolism are given in table 156 herewith. Owing to a defect in the apparatus the heat eliminated between $10^h\ 12^m$ a. m. and $12^h\ 12^m$ p. m. can not be advantageously separated into hourly periods, but we have every reason to believe that the total heat measured for the 2 hours from $10^h\ 12^m$ a. m. to $12^h\ 12^m$ p. m. is correct, and the total heat for these two periods is therefore given in the table.

A similar defect was experienced in the measurement of the oxygen consumption, for as has been pointed out in previous publications,[1] the determination of the amount of oxygen consumed depends in large part upon an accurate temperature measurement. Consequently, the total oxygen consumption for the 2 hours is given in the table rather than the amount consumed in each hour.

TABLE 156.—*Measurements of metabolism—Metabolism experiment No. M 2.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
April 24, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
$9^h\ 12^m$ a.m. to $10^h\ 12^m$ a.m.	24.5	24.0	208	280	29.2	0.74	88	77	14
10 12 a.m. 11 12 a.m.	22.6	43.0	192	251	29.9	.78	179	74	14
11 12 a.m. 12 12 p.m.	23.5		199		30.5			74	13
12 12 p.m. 1 12 p.m.	23.8	21.2	202	247	28.9	.81	81	74	13
Total 4 hours[1].....	94.4	88.2	200	257	118.5	....	[2]348	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 2.41 c. c.; oxygen absorbed per kilogram per minute, 3.09 c. c.; heat eliminated per kilogram per hour, 1.05 calories.
[2] Rectal body-temperature at beginning, 36.90° C.; at end, 37.04° C. Heat production for total 4 hours, 358 calories.

The experiment appeared to be successful in every way and the subject found the sojourn in the chair calorimeter pleasanter than in the bed calorimeter. As is customary in most experiments, the pulse-rate was somewhat higher in the first period, the values given in the table representing the average of a number of observations for each 1-hour period. The respiration-rate, as is commonly the case, underwent minor fluctuations, although in this particular experiment the fluctuations were larger than usual; the figures given represent the average of a number of observations for each hour.

METABOLISM EXPERIMENT No. M 3.

Date, November 27, 1909. Naked body-weight, 81.4 kilograms.

In the period intervening between this and the preceding experiment, the subject had personally regulated his diet, but had not been under hospital régime. As the clinical picture had not materially altered, it seems of value to note any possible changes in his case as evidenced by the metabolism.

[1] Benedict and Milner, U. S. Dept. Agri., Office Exp. Sta. Bul. 175, 1907, pp. 23–32. Benedict, Am. Journn. Physiol., 1910, **26**, p. 15.

He came to the laboratory in the morning without breakfast and entered the chamber of the chair calorimeter at 8h 01m a. m. The experiment began at 8h 45m a. m. and continued for three 1-hour periods, ending at 11h 45m a. m. During the experiment proper, no urine was passed and no water consumed. Although the subject was fairly quiet, he reported at the end of the experiment that he found the chair somewhat uncomfortable, and that the rectal thermometer irritated him slightly. As previously, the pulse- and respiration-rates were obtained by means of the stethoscope and pneumograph, and ranged from 76 to 79 and from 12 to 15, respectively. The body-temperature was measured by the electrical-resistance thermometer.

The muscular activity was at a minimum during the last period, and the observer's records show that during a part of the period he was asleep.

TABLE 157.—*Measurements of metabolism—Metabolism experiment No. M 3.*

Date and period.	Carbon dioxide eliminated.	Oxygen absorbed.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Water vaporized.	Respiratory quotient.	Heat eliminated.	Average pulse-rate.	Average respiration-rate.
November 27, 1909.	*gms.*	*gms.*	*c. c.*	*c. c.*	*gms.*		*cals.*		
8h 45m a.m. to 9h 45m a.m.	22.7	23.0	193	268	24.0	0.71	74	78	13
9 45 a.m. 10 45 a.m.	22.4	22.0	190	257	24.9	.74	76	77	14
10 45 a.m. 11 45 a.m.	21.9	22.0	186	257	24.8	.72	70	77	13
Total 3 hours[1]	67.0	67.0	189	261	73.7	....	[2]220	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 2.32 c. c.; oxygen absorbed per kilogram per minute, 3.20 c. c.; heat eliminated per kilogram per hour, 0.90 calories.
[2] Rectal body-temperature at beginning, 36.67° C.; at end, 36.89° C. Heat production for total 3 hours, 235 calories.

The results of the metabolism are given in the table 157. As in the other experiments the averages for the pulse- and respiration-rates indicate the average from a number of observations on this subject. The metabolism as a whole, as indicated by the carbon-dioxide elimination, oxygen consumption, and heat-elimination was somewhat low during the last period, this being in conformity with the noticeably decreased muscular activity shown by the pneumograph record for this period.

COMPARISON OF EXPERIMENTS WITH CASE M.

While the course of the disease with this subject may be traced in a general way from the chart given on a preceding page, it is of interest to compare the records of the metabolism in the three experiments made with this individual. The comparison is of value in indicating first, the constancy of metabolism with this subject, and second, any noticeable variations incidental to any change in the method of conducting the experiments. The results for the three experiments with this subject are given in table 158.

TABLE 158.—*Comparison of metabolism experiments with Case M.*

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Respiratory quotient.	Heat eliminated per hour.	Heat produced per hour.	Average pulse-rate per minute.	Average respiration per minute.
	1909.	*kilos.*	*hrs.*	*c. c.*	*c. c.*		*cals.*	*cals.*		
M 1	Feb. 27[1]......	81.8	3	210	268	0.78	81	80	..	11.5
M 2	Apr. 24.......	83.1	4	200	257	.78	87	89	75	13.5
M 3	Nov. 27.......	81.4	3	189	261	.72	73	78	77	13.5

[1] Bed calorimeter.

Of these experiments, the first was made in the bed calorimeter and one would therefore expect to find that the metabolism was less during rest than in the other two experiments when the subject was sitting up. On the other hand, in the last experiment there was a period of time when he was without doubt asleep and the muscular activity was very small. The carbon-dioxide elimination per minute was highest in the first experiment and lowest in the last, while there was practically no variation in the oxygen consumption. The lowest heat-elimination was in the last experiment and the highest in the second.

It is also feasible here to make a comparison of the heat-production in the different experiments. The values recorded in this column were obtained by dividing the total heat-production for each experiment by the number of hours the experiment continued. This total heat-production takes into consideration the changes in body-temperature, and is therefore affected by any errors incidental to the body-temperature measurement. However, for periods of 3 to 6 hours, we believe that the heat-production may be used advantageously for comparison with the respiratory exchange.

There is a perceptible difference in the respiration-rate when the subject was sitting in the chair as compared with the period when he was lying on the bed. Perhaps the most noticeable feature in this series of experiments is the fact that in the third experiment, the respiratory quotient was considerably lower than in the other two experiments. As pointed out in a subsequent section this factor is of special significance in diabetes as indicating the status of the disease. During this last experiment, judging from the respiratory quotient, it would appear that the supply of reserve carbohydrate in the body of the subject was considerably less than in the first two experiments. The respiratory quotient would indicate a metabolism wholly of fat, and yet there was no marked acidosis. In this special case, despite the absence of a large amount of sugar in the urine, there was apparently only a low storage of glycogen in the body.

It is important here to note that the direct determination of the heat-elimination, when compared with the indirect determination, does not show the concordance that one would expect. Assuming the calorific value of oxygen with

a respiratory quotient of 0.78 as 4.78 calories, we would expect in the first experiment a larger heat-elimination than in the second, in which some 4 per cent less oxygen was consumed, whereas an examination of the data for the heat-elimination and heat-production indicates an increased heat-production in the second experiment over the first, varying from 7 to 10 per cent. On the other hand, in the last experiment there was a noticeable fall in the heat-production, with a slight rise in the oxygen consumption. It has not yet been demonstrated that in short experiments the direct and indirect heat-determinations agree closely with people in normal health and with normal metabolism. It is evident from these experiments that we have here such conditions as preclude the possibility of computing accurately the heat-production from the respiratory exchange. So far as this experiment is concerned one can only state that the direct and indirect calorimetry are not in accord.

It is perhaps a little surprising that there should be such a perceptible decrease in both the oxygen consumption and the carbon-dioxide elimination in the experiments with the chair calorimeter as compared with that in which the bed calorimeter was used, for obviously the patient was quieter in the bed calorimeter. On the other hand, it has been the frequent experience in this series of experiments that in the first experiment the novelty of the experience produces an excitability and muscular tonus that tend to a higher heat-production and a generally higher metabolism.

PART III.

DISCUSSION OF RESULTS AND GENERAL CONCLUSIONS.

The data presented in the preceding section are summarized and discussed in the following pages. In this discussion the grouping differs slightly from that used in the statistics as the cases are considered in only two classes, *i. e.*, severe diabetes (Cases A to J) and light diabetes (Cases K to M).

In general, the method of treatment used for the discussion in this publication is the same as in preceding publications of this nature, that is, the more obvious comparisons and summaries are first taken up, a general summary is then made of the various relations of metabolism, and, finally, some general conclusions are drawn and the needs for further investigations are pointed out. It is not to be presumed that all of the possible topics in relation to the metabolism in diabetes are dwelt upon, but those which are more apparent are considered.

PULSE-RATE.

Several thousand observations of the pulse-rate were made on these subjects at different times and while, as pointed out in the statistical discussion with each subject, there are numerous relatively wide variations, particularly with Case A, on the whole the pulse-rate of the subjects remained well within the normal limit. The unusually high pulse-rate of Case I, which averaged in one experiment 122 per minute and in the other 118, has been the subject of special comment in another part of this report.[1] Case A had a pulse-rate varying from 65 per minute in experiment A 3 to 95 per minute in experiment A 15, after eating meat. Even without food the pulse-rate at times rose to 90, as in experiment A 5a. The fluctuations in pulse-rate obtained by this subject have also been especially commented on. Other than the two variations mentioned above, the pulse-rate for all the subjects was well within normal bounds.

RESPIRATION-RATE.

By means of the pneumograph, the respiration-rate could be obtained with great accuracy and with considerable regularity. The records all show reasonable uniformity with the same subject from experiment to experiment, and with no subject were abnormal respiratory rates found. In other words, we have no reason for assuming that diabetes has any influence whatever on the respiration-rate when subjects are resting quietly, either lying on the couch or bed or sitting in a chair.

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[1] See p. 129.

BODY-TEMPERATURE.

In practically all of the cases here studied, the temperature was measured frequently. At times it was measured every few minutes by an electrical-resistance thermometer; in other experiments clinical thermometers, carefully calibrated, were used and the temperature taken by the subject under the tongue. Of the several hundred observations made on these subjects, there was in no instance an indication of an abnormal temperature at the time the experiments were carried out, and in so far as the observations extended over different periods of the day, the minor fluctuations in rectal temperature, as indicated by the electrical-resistance thermometer, were parallel in general with those found on normal subjects.

CHANGES IN BODY-WEIGHT.

Practically all of the diabetic subjects who were used in these experiments had lost in weight as compared with their former best weights. Inasmuch as Magnus-Levy has pointed out that there may be a disturbance of the relationship between body-surface and body-weight with emaciated subjects, it is of interest to note to what degree these different subjects became emaciated. Consequently, their greatest naked body-weights in health and the lowest weights recorded during the experiments have been collected in table 159. With nearly all of the subjects, this lowest weight represents, probably, the average weight of the body at this time. As a matter of fact in some of the experiments, particularly with Case A, there were noticeable increases in weight, which as has been stated before, may be wholly due to edema. On the other hand, with Case C there was unquestionably a distinct loss in weight from June until the following fall, which could not be attributed simply to a loss of water as the result of a disappearing edema.

TABLE 159.—*Comparison of body-weights of subjects in health and disease.*

Subject.	Greatest body-weight in health.	Minimum weight during experiments.	Loss in body-weight.	Per cent loss of original best weight.
	kilos.	*kilos.*	*kilos.*	*p. ct.*
Case A.........	68.0	48.8	19.2	28
Case B.........	50.7	40.5	10.2	20
Case C.........	75.9	54.9	21.0	28
Case D.........	57.3	48.0	9.3	16
Case F.........	80.5	59.0	21.5	27
Case G.........	73.6	67.1	6.5	9
Case H.........	57.7	51.8	5.9	10
Case I.........	56.8	45.1	11.7	21
Case J.........	59.1	53.7	5.4	9
Case K.........	73.2	60.6	12.6	17
Case L.........	79.1	63.0	16.1	20
Case M.........	86.4	81.4	5.0	6

It is thus seen that some of these subjects lost in weight very considerably and others only moderately. The greatest loss was that of Case F of 21.5 kilograms. While the largest losses in weight were usually among severe cases, yet two of the three lighter cases, K and L, showed 17 to 20 per cent loss, thus indicating that the severity of the case *per se* is without influence on the degree of emaciation.

The use of body-weight as an index of the physical condition of diabetics is the source of many errors, for changes in body-weight, to be of real significance, should indicate loss or change of organized tissue or fat. Fluctuations in body-weight due to changes in the water content of the body are not of vital significance from the standpoint of the supply of energy, in taking the calories as a whole. Thus it may frequently happen that on an extraordinarily low energy diet, when actually the subject was not getting sufficient energy to maintain the body in energy equilibrium, there may be a gain in weight due to some phase in the treatment. For instance, the administration of sodium bicarbonate may result in an edema which would entirely mask the loss in weight taking place every day through the deficiency in the diet and this loss must be supplied from the body-material.

The gain in weight shown by Case A [1] between November 2, 1908, 47.7 kilograms, and November 11, 1908, 53.3 kilograms, was undoubtedly due in part to the retention of water which has been shown by Joslin and Goodall [2] to take place in severe diabetes when the diet is restricted and sodium bicarbonate administered. This was also marked in other cases, Case D, for instance, gaining 3.5 kilograms in 8 days.[3] It has been known for some time that rapid gain in weight due to edema takes place on von Noorden's oatmeal diet, but it has not been so well recognized that this occurs independently of such a diet in severe diabetes. The work of Joslin and Goodall suggests that this is brought about by a retention of salt caused by the irritation of the kidneys which the increasing acidosis, consequent upon a restricted diet, induces. It is not dependent upon, but is accentuated by the administration of sodium bicarbonate, because in this way more acid is washed out through the kidneys. For these reasons, calculations upon the energy requirements of diabetic patients based upon weight must be considered only approximate. In recognition of this fact, weights of patients have been recorded in this report only to tenths of kilograms.

It is highly probable that sudden increases in body-weight, whenever they occur, are due solely to edema and do not represent any actual gain of body-tissue. On the other hand, a loss of body-weight of several kilograms extending over several months' time can not be taken as indicating merely the loss in water and may actually and probably does involve a loss of organized tissue.

Recently a case has been called to our attention in which the edema in a severe

[1] See table 9, p. 39.
[2] Joslin and Goodall, Journ. Am. Med. Asso., **51**, pp. 727-731.
[3] September 29, to October 6, 1909. See table 88, p. 94.

case of diabetes became so extreme that a physician of experience reported it to be greater than any edema he had ever before witnessed. At one time it was thought that tracheotomy would be necessary. Upon investigation it was found that the patient had taken 1 kilogram of sodium bicarbonate in the preceding week. During treatment he was given adrenalin, and subsequently the edema disappeared. The patient lived for a year longer and finally died of diabetic gangrene.

BODY-SURFACE.

It is quite common to compare the metabolism of different individuals in health on the basis of per kilogram of body-weight or per square meter of body-surface. According to Rubner, the metabolism is proportional to the body-surface, which is found from the body-weight by using the formula of Meeh[1]: $12.312 \sqrt[3]{\text{body-weight}}$.

In discussing the metabolism of diabetics, Magnus-Levy has made the claim that while the metabolism per kilogram of body-weight may be larger than normal, as a matter of fact, the comparison should be made not with a normal individual of the same body-weight, but with an individual having the original weight of the diabetic when in health, as the diabetic would have wasted away as a result of the disease. In support of this argument, he states that this loss in body-weight may not have been followed by a proportionate change in body-surface, and the body-surface is therefore larger as compared with the body-weight than it was before the diabetic became emaciated. He further claims that if the metabolism is proportional to the body-surface, a diabetic ought to show relatively the same absolute amount of metabolism irrespective of body-weight.

This argument of Magnus-Levy is not tenable for several reasons. First, a marked loss in weight by diabetics is not accompanied by the apparent increase in skin area in proportion to the body-weight which is shown by elderly people who have shrunk and lost in weight from causes other than diabetes. Furthermore, it is by no means proved that the shrinking in body-weight experienced by elderly people does really leave a materially increased body-surface in proportion to the body-weight, for as the skin shrivels and falls into folds, there is unquestionably less area for the radiation of heat. If the skin area in age remains larger in proportion to the body-weight than with normal individuals, then, if the assumption is true that the metabolism is proportional to and determined by the area of the skin, we would expect a larger metabolism per kilogram of body-weight with elderly people than with young people, and, as a matter of fact, this is contrary to actual experience.

With the diabetics used in our experiments, all of whom were comparatively young, there was no appearance of the skin lying in folds, nor any evidence that

[1] Meeh, Zeitschr. f. Biol., 1897, 15, p. 425.

the skin area was larger in proportion to the body-weight than in health. It would appear, therefore, that although these diabetics showed a marked loss in body-weight, amounting to as much as 27 to 28 per cent, there was, without doubt, a compensating shrinkage of the skin so that the skin area remained proportionately the same per kilogram of body-weight as in health.

THE GASEOUS EXCHANGE AND ENERGY TRANSFORMATIONS IN PERIODS WITHOUT FOOD.

In experiments on the gaseous exchange in diabetes, the one factor that has been measured more than any other has been the carbon-dioxide excretion, and in experiments with diabetics as well as with normal individuals, an attempt has been made by investigators to estimate the heat-production from the carbon-dioxide elimination.

SIGNIFICANCE OF THE CALORIFIC EQUIVALENT AND THE RESPIRATORY QUOTIENT.

As oxygen is taken into the lungs and carried by the blood to the various tissues, it combines with body-material to form carbon dioxide and water in the normal processes of metabolism, and in so doing heat is liberated. From a large number of experiments the amount of heat per gram of carbon dioxide produced and the amount of heat per gram of oxygen absorbed have been computed. An examination of the calorific equivalents of carbon dioxide and oxygen shows, however, that while the number of calories accompanying the absorption of each gram of oxygen is nearly the same whether protein, fat, or carbohydrate is oxidized, on the other hand, the number of calories accompanying the production of each gram of carbon dioxide varies noticeably with the different materials burned, the extremes being indicated by carbohydrate and fat, protein occupying an intermediate position. Consequently, if the carbon-dioxide elimination in normal individuals is taken as an index of the total energy transformation, an error is introduced.

Furthermore, the absorption of each gram of oxygen results in the formation of a definite amount of carbon dioxide, and this amount also varies very considerably with the nature of the material burned. From the ratio of the oxygen absorbed to the carbon dioxide given off, *i. e.*, the respiratory quotient, many interesting conclusions as to the nature of the metabolism may be drawn.

When carbohydrate is oxidized, it can be seen from the chemical structure of the molecule ($C_6H_{12}O_6$), that there is sufficient oxygen in the molecule of itself to completely combine with the hydrogen and form water, leaving practically only carbon to be oxidized. It is, of course, obvious that there is not such a sharp division in the cleavage of the carbohydrate molecule that the oxygen preexisting in the molecule invariably combines with the hydrogen, but the end result is the same, namely, that when carbohydrates are oxidized, the amount of oxygen required is measured by the amount of carbon in the molecule. Since

in the conversion of carbon to carbon dioxide, for every liter of oxygen absorbed, there is produced 1 liter of carbon dioxide, obviously, in any chemical transformation where carbohydrate alone is burned, the volume of carbon dioxide produced is equivalent to the volume of oxygen absorbed.

With normal individuals the combustion of carbohydrate is a very important factor, and, indeed, many diets, particularly in the warmer climates, consist almost exclusively of carbohydrates. On the other hand, in dealing with diabetics, where the metabolism is largely of fat, the relationship between the oxygen absorbed and the carbon dioxide produced when fat is burned is of more direct significance and importance. An examination of the structure of the molecule of fat shows that there is a relatively small amount of preexisting oxygen. Consequently, when fat is burned in the body, a considerable amount of oxygen is required to convert not only the carbon to carbon dioxide but also the hydrogen of the molecule to water, since there is so small an amount of oxygen available in the molecule itself for this oxidation.

Here again, it is not permissible to assume that the oxidation travels in any definite line, or that the oxygen of the molecule has any selective function in combining with this or that hydrogen or carbon atom, but assuming that all the oxygen of the molecule is completely combined with the hydrogen, it can be seen from a computation of the molecular weights that the oxygen is still insufficient to completely oxidize the hydrogen molecule. Consequently, when oxygen is absorbed from the air in the combustion of fat, it is used not only in the formation of carbon dioxide but likewise to form a certain amount of water, and a much larger volume of oxygen is thus absorbed than of carbon dioxide produced. When pure fat is burned, it has been computed that for every liter of oxygen absorbed, there are 711 c. c. of carbon dioxide produced.

In addition to the combustion of fat which plays so important a rôle in diabetes, we have also a large disintegration of protein. With diabetics this disintegration is fully as large as with normal individuals, and in many instances, when a special diet is administered, it is much larger. While the disintegration of carbohydrate and fat proceeds with relatively simple processes of oxidation, the apportionment of the oxidation between carbon and hydrogen is much more difficult when protein is disintegrated, owing to the extremely complex nature of the protein molecule. The nitrogen of the protein is excreted in the form of urinary products, and it has been definitely proved that no nitrogen leaves the body as nitrogen gas. There have been a number of methods for computing the proportion of oxygen absorbed to carbon dioxide produced in the combustion of protein, but perhaps the best is that presented by Loewy.[1] By this method he computes that for every liter of oxygen absorbed there are 801 c. c. of carbon dioxide produced.[2]

[1] Loewy, Oppenheimer's Handbuch der Biochemie des Menschen und der Thiere, Jena, 1908, **4**, p. 156.

[2] For a complete discussion of this point see Benedict and Carpenter, Publication No. 126, Carnegie Institution of Washington, 1910, pp. 209-212.

Some general idea of the relations existing among the amounts of oxygen, carbon dioxide, and heat accompanying the oxidation of various materials in the body may be obtained from table 160. From these values it is clear that if we know the relationship between the carbon dioxide produced and oxygen consumed, and furthermore, if we know the heat measured, it is possible to estimate with considerable accuracy the nature both qualitatively and quantitatively of the katabolism itself. Thus, if in an experiment the respiratory quotient, or the relationship between the carbon dioxide produced and the oxygen absorbed, is 0.95, the indications are that during the period in which the experiment was in progress the material burned was in large part of a carbohydrate nature, while, on the other hand, if we find a ratio of approximately 0.72, as is frequently the case with diabetics, obviously the material katabolized consisted largely of fat.

TABLE 160.—*Respiratory quotients and calorific equivalents of carbon dioxide and oxygen for protein, fats, and carbohydrates.*

Materials.	Oxygen required to oxidize 1 gram.		Products of the oxidation of 1 gram.				Respiratory quotient.	Calorific equivalent of 1 gram.	
			Carbon dioxide						
	Weight.	Volume.	Weight.	Volume.	Water.	Heat.	$\frac{CO_2 \text{ c. c.}}{O_2 \text{ c. c.}}$	Of carbon dioxide produced.	Of oxygen required.
	grams.	*c. c.*	*grams.*	*c. c.*	*grams.*	*cals.*		*cals.*	*cals.*
Starch	1.185	829.5	1.629	829.3	0.556	4.20	1.000	2.58	3.55
Cane sugar.	1.122	785.4	1.543	785.5	.579	3.96	1.000	2.56	3.53
Glucose	1.066	746.2	1.466	746.2	.600	3.75	1.000	2.56	3.52
Animal fat.	2.876	2013.2	2.811	1431.1	1.065	9.50	.711	3.38	3.30
Human fat.	2.844	1990.8	2.790	1420.4	1.055	9.54	.713	3.42	3.36
Protein	1.367	956.9	1.520	773.8	.340	4.40	.809	2.90	3.22

THE GASEOUS EXCHANGE AND ENERGY TRANSFORMATIONS OF NORMAL INDIVIDUALS.

Of fundamental importance is the comparison of the metabolism of diabetics with normal individuals. In making such comparisons, however, it is important that possible variations in body activity, state of digestion, body-weight, body-surface, and similar factors should be taken into consideration. It is relatively easy to make experiments with selected normal individuals in which the muscular activity is approximately the same as in experiments with diabetics, thus eliminating the influence of this factor. Secondly, by making experiments on normal individuals 12 hours or more after the last meal, the results will not be complicated by the ingestion of food. On the other hand, when we compare normal individuals and diabetics on the basis of per kilogram of body-weight and per square meter of body-surface, we find certain abnormalities that are very difficult to adjust, and consequently we are not able to make a wholly satisfactory comparison in this way.

The metabolism of normal men of varying ages, body-weights, and other physical characteristics has been studied extensively by Magnus-Levy and Falk,[1] Sondén and Tigerstedt,[2] and more recently by Benedict and Carpenter.[3] The values found by Magnus-Levy and Falk have especial significance for comparison with values obtained in experiments with diabetic individuals in which the respiration apparatus is used or the bed calorimeter, for their experiments were all made with subjects lying on a couch with enforced muscular rest. On the other hand, the experiments of Benedict and Carpenter are peculiarly adapted for comparison with subjects inside of the chair calorimeter, as a large majority of their experiments were made with individuals sitting quietly in a chair reading. They also report a large number of experiments with individuals sleeping, between 1 a. m. and 7 a. m. Unfortunately, the sleeping experiments of Benedict and Carpenter are not strictly comparable with the experiments made on diabetics with the respiration apparatus or in the bed calorimeter, since with the sleeping experiments in a large number of instances, the period began but 6 or 7 hours after the last meal, while in most of the new experiments on diabetics here reported the beginning of the period was at least 12 hours after the last meal—frequently 14 hours. However, it is quite probable that the digestive processes had largely ceased during the sleeping period in the respiration chamber of Wesleyan University, and hence these values have considerable significance when compared with the results of the diabetic experiments without food.

THE GASEOUS EXCHANGE OF NORMAL INDIVIDUALS AS DETERMINED WITH THE ZUNTZ-GEPPERT APPARATUS.

The values found with the Zuntz-Geppert apparatus, drawn in large part from the researches of Magnus-Levy and supplemented by researches of others of the Zuntz school, are given in table 161, which is abstracted from the table given by Loewy.[4] The subjects are arranged in order of the increasing body-weights.

It is clearly shown in this table that appreciable differences exist in the metabolism of different individuals, even among those having approximately the same body-weight, with enforced muscular quiet and 12 hours after the ingestion of food, as is the rule in experiments with the Zuntz-Geppert apparatus. This is strikingly shown with Subjects 10 and 11. With Subject 10, with a body-weight of 61.2 kilograms, the oxygen consumption was 5.50 c. c. per minute and the carbon-dioxide elimination 4.18 c. c., while with Subject 11, with a body-weight of nearly 4 kilograms greater, the oxygen consumption was 3.39 c. c., and the carbon-dioxide production 2.50 c. c. In general, however, the smaller the body-

[1] Magnus-Levy and Falk, Archiv f. Anatomie und Physiologie. Physical. Abthg., Supplementband, 1899, p. 314.
[2] Sondén and Tigerstedt, Skand. Archiv. f. Physiologie, 1895, 6, p. 1.
[3] Benedict and Carpenter, Publication No. 126, Carnegie Institution of Washington, 1910.
[4] Loewy, Oppenheimer's Handbuch der Biochemie des Menschen und der Thiere, Jena, 1908, 4, p. 179.

weight the higher the production of carbon dioxide and the oxygen consumption per kilogram of body-weight.

TABLE 161.—*Gaseous exchange per minute of normal individuals as determined with the Zuntz-Geppert apparatus.*

No.	Age.	Body-weight.	Per kilo. of body-weight per minute. Carbon dioxide eliminated.	Per kilo. of body-weight per minute. Oxygen consumed.
	years.	*kilos.*	*c. c.*	*c. c.*
1	24	43.2	3.40	4.53
2	24	48.0	2.88	3.68
3	30	50.8	3.08	3.73
4	36	53.0	3.45	4.14
5	24	56.3	3.21	4.41
6	56	56.5	2.98	3.93
7	32	58.0	2.90	3.81
8	(?)	58.5	3.05	3.96
9	38	60.0	2.96	3.80
10	(?)	61.2	4.18	5.50
11	43	65.0	2.50	3.39
12	(?)	66.1	2.60	3.42
13	25	67.5	2.86	3.43
14	22	67.5	2.97	3.43
15	23	71.7	2.96	3.73
16	34	73.6	2.66	3.37
17	34	82.0	2.17	2.76
18	29	82.7	2.72	3.60
19	22	88.3	2.69	3.30
Average	..	63.7	2.96	3.79

THE GASEOUS EXCHANGE OF NORMAL INDIVIDUALS DURING SLEEP IN THE RESPIRATION CALORIMETER.

In the large number of experiments made with the respiration calorimeter at Wesleyan University in which the gaseous exchange between 1 a. m. and 7 a. m. was studied, 19 different subjects were used. In the majority of these experiments the oxygen consumption was directly determined as well as the carbon-dioxide production. The values found for these different individuals per kilogram of body-weight per minute are given in table 162.

An examination of this table shows that the variations in the carbon-dioxide elimination do not bear a definite relation to the body-weight, although with the subject W. O. A., with a body-weight of 84.7 kilograms, there is the lowest carbon-dioxide elimination per kilogram of body-weight, and one of the highest amounts eliminated is found with the subject H. E. S., with a body-weight of but 56.6 kilograms. On the other hand, when the results for oxygen consumption are examined, it is seen that, in general, the lower the body-weight the higher the oxygen consumption, although there is not a strictly mathematical relationship between these.

TABLE 162.—*Gaseous exchange by different individuals during sleep in the respiration chamber at Wesleyan University.*
(1 a. m. to 7 a. m.)

Subject.	Age.	Weight.	Height.	Per kilo. of body-weight per minute. Carbon dioxide eliminated.	Per kilo. of body-weight per minute. Oxygen consumed.
	years.	*kilos.*	*cms.*	*c. c.*	*c. c.*
W. O. A.	59	84.7	168	2.35	2.92
D. W.	22	78.3	180	2.88	3.61
J. C. W.	26	77.1	178	2.92	3.71
H. C. K.	22	72.0	181	2.92	3.55
A. L. L.	25	71.5	156	3.03	3.78
H. F.	53	71.2	168	2.61	3.27
A. W. S.	23	69.4	176	2.94	....
E. O.	32	68.3	173	2.83	....
N. M. P.	21	66.9	177	3.12	3.79
B. F. D.	23	66.4	170	2.95	3.54
C. R. Y.	20	66.1	170	3.22	3.87
H. A.	19	64.1	170	3.64	4.70
J. F. S.	29	64.0	171	2.98	....
A. H. M.	24	61.6	179	2.67	3.53
O. F. T.	24	57.2	168	3.56	....
S. A. B.	23	57.0	166	2.96	3.61
H. E. S.	19	56.6	178	3.41	4.66
H. R. D.	18	56.2	171	3.18	3.99
H. L. K.	24	55.0	166	2.99	3.75
Average	27	66.6	172	3.01	3.75

VARIATIONS IN METABOLISM DURING SLEEP DUE TO VARIATIONS IN PHYSICAL CHARACTERISTICS.

Recognizing these differences in individuality and in body-weight, Benedict and Carpenter have collected into groups a number of these experiments and characterized the subjects as short, fat men, lean men, tall men, and short men, respectively. The results of these experiments are given in table 163. The values given in this table are for the period from 1 a. m. to 7 a. m., when the subjects were lying quietly asleep on a bed inside of the respiration chamber, and at least 7 hours after the last meal was taken.

The individuals selected in these groups are not numerous enough to draw deductions from, but it seems clear that there is a marked difference in metabolism per kilogram of body-weight between the short, fat men and the lean men, while the values for the tall men and short men range between these two groups. These variations are defined with sufficient sharpness to indicate a marked difference in the metabolism, and the differences in the body-condition should, therefore, be taken into consideration when making any comparison.

These variations in metabolism due to physical characteristics make a comparison between diabetics and normal individuals all the more difficult, since diabetics are frequently considerably reduced in body-weight and are more or less emaciated. This is particularly true with Case I in the diabetic experiments here reported, who was a tall man but with a very small body-weight.

TABLE 163.—*Comparison of gaseous exchange during sleep of subjects grouped according to physical characteristics.*

Group and subject.	Body-weight (without clothing).	Height.	Per kilo. of body-weight per minute. Carbon dioxide eliminated.	Oxygen absorbed.
Group I.—Short, fat men:	*kilos.*	*cms.*	*c. c.*	*c. c.*
W. O. A.	74.7	168	2.35	2.92
H. F.	71.2	168	2.61	3.27
Group II.—Lean men:				
H. E. S.	56.6	178	3.41	4.66
H. R. D.	56.2	171	3.18	3.99
Group III.—Tall men:				
H. C. K.	72.0	181	2.92	3.55
D. W.	78.3	180	2.88	3.61
A. H. M.	61.6	179	2.67	3.53
Group IV.—Short men:				
O. F. T.	57.2	168	3.56	....
A. L. L.	71.5	166	3.03	3.78
S. A. B.	57.0	166	2.96	3.61
H. L. K.	55.0	166	2.99	3.75

In his discussion on diabetes, Magnus-Levy has attempted to compare the metabolism of each individual with a normal individual of approximately the same body-weight and general condition. In view of the preceding statements with regard to the marked difference in metabolism between two men of approximately the same body-weight such a comparison is hardly permissible, and it is obvious that in this discussion we must deal with groups of individuals rather than with individuals. It is probably true that with all the diabetics used as subjects in the experiments here reported, with the possible exception of Case M, there is a greater degree of emaciation than with normal individuals, and in the statistical statements regarding these individuals, we will find evidence that their former body-weight was considerably greater than the body-weight at the time of the experiment. Certain individuals may be classified as lean men, and, therefore, we would expect normally a high metabolism, while other subjects, from the measurements of body-weight and height, would not appear to be greatly emaciated, and hence are comparable to the group of individuals designated as short men.

COMPARISON OF THE RESULTS OBTAINED WITH THE ZUNTZ-GEPPERT APPARATUS AND WITH THE RESPIRATION CALORIMETER DURING SLEEP.

Very recently, Durig[1] has brought together a large number of experiments made with the Zuntz-Geppert apparatus, and also has included a number of experiments made with the respiration calorimeter at Wesleyan University.

[1] Durig, Physiologische Ergebnisse der in Jahre 1906 Durchgeführten Monte Rosa-Expedition. Ueber den Erhaltungsumsatz. Besonders Abgedruckt aus dem LXXXVI. Bande der Denkschriften der Mathematisch-Naturwissenschaftlichen Klasse der Kaiserlichen Akademie der Wissenschaften, Wien, 1909.

Seventeen subjects experimented on with the Zuntz-Geppert apparatus are compared with 10 subjects in the respiration calorimeter. Unfortunately, the comparison is not as obvious as would appear from Durig's figures, inasmuch as he included seven experiments with one subject who was used in a number of fasting experiments. The comparisons as made by Durig show an average oxygen consumption per kilogram of body-weight per minute of 3.53 c. c. with the Zuntz-Geppert apparatus as compared with 3.55 c. c. with the respiration calorimeter, and a carbon-dioxide production of 2.83 c. c. with the Zuntz-Geppert apparatus against 2.91 c. c. with the respiration calorimeter.

GASEOUS EXCHANGE AND ENERGY TRANSFORMATIONS IN RECENT CONTROL EXPERIMENTS ON NORMAL INDIVIDUALS.

While the results of these earlier investigations supply considerable data regarding normal metabolism as a basis of comparison with the results of experiments made with diabetics, yet a comparison of the metabolism of individuals during experiments in different laboratories and with different forms of apparatus is at best unsatisfactory. Therefore, in connection with the investigation on the metabolism of diabetics here reported, control experiments have also been made on normal individuals 12 hours after the last meal with all three forms of apparatus. With the chair calorimeter we have a series of experiments with several individuals and the results of these experiments are given in table 164. The variations range from 2.66 c. c. of carbon dioxide eliminated per kilogram per minute to 4.20 c. c., the oxygen consumption from 3.07 c. c. to 5.15 c. c., and the heat eliminated per hour per kilogram 0.97 calories to 1.47 calories. The average of all the subjects gives the carbon-dioxide production as 3.26 c. c., oxygen consumption, 3.99 c. c., and heat elimination, 1.21 calories per hour per kilogram of body-weight.

TABLE 164.—*Average metabolism of normal individuals in experiments without food. (Chair calorimeter.)*

Subject.	Body-weight (without clothing).	Height.	Total number of hours.	Per kilo. of body-weight per minute.		Heat eliminated per kilo. of body-weight per hour.
				Carbon dioxide eliminated.	Oxygen absorbed.	
	kilos.	*cms.*		*c. c.*	*c. c.*	*cals.*
Prof. C.	83.5	169	4	3.15	3.63	1.12
H. F.	79.7	166	3	2.71	3.07	0.97
F. A. R.	74.4	163	18	3.27	4.12	1.17
J. J. C.	67.6	175	5	3.29	4.02	1.34
Mrs. B.	67.0	161	2	2.66	3.48	1.09
Dr. H.	66.5	182	4	2.79	3.56	1.12
J. R.	66.0	182	12	3.47	4.21	1.20
L. E. E.	59.6	179	11	4.20	5.15	1.47
Dr. R.	48.5	167	4	3.76	4.67	1.39
Average	....	....	..	3.26	3.99	1.21

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A series of experiments with fewer subjects was likewise made with the bed calorimeter, and these results are given in table 165. While the variations in the body-weights of the subject are nearly as great as those in the experiments with the chair calorimeter, the ranges in the values for carbon-dioxide elimination and oxygen consumption are not as great, the average values for carbon dioxide being 2.95 c. c., for oxygen, 3.51 c. c., and 1.01 calories per kilogram of body-weight per hour.

TABLE 165.—*Average metabolism of normal individuals in experiments without food.* (*Bed calorimeter.*)

Subject.	Body-weight (without clothing).	Height.	Total number of hours.	Per kilo. of body-weight per minute.		Heat eliminated per kilo. of body-weight per hour.
				Carbon dioxide eliminated.	Oxygen absorbed.	
	kilos.	*cms.*		*c. c.*	*c. c.*	*cals.*
F. G. B	83.0	183	4.5	2.76	3.23	1.01
F. A. R	74.4	163	10	2.77	3.34	.95
J. J. C	67.6	175	22.5	2.86	3.36	.96
J. R.	66.0	182	6	2.94	3.59	1.00
T. M. C	49.0	166	5	3.43	4.05	1.13
Average	....	....	....	2.95	3.51	1.01

Experiments with six different individuals on the respiration apparatus also furnish a basis for comparison. These are given in table 166. The variations in the body-weights of the different subjects are about the same as in the bed calorimeter experiments.

TABLE 166.—*Average gaseous exchange of normal individuals per kilogram per minute in experiments without food.* (*Respiration apparatus.*)

Subject.	Body-weight (without clothing).	Height.	Total number of experiments.[1]	Per kilo. of body-weight per minute.	
				Carbon dioxide eliminated.	Oxygen absorbed.
	kilos.	*cms.*		*c. c.*	*c. c.*
F. G. B	82.0	183	1	2.67	3.30
F. A. R	74.4	163	1	2.67	3.15
J. R.	66.0	182	11	3.06	3.68
J. J. C	65.6	175	8	2.87	3.52
L. E. E	59.0	179	13	3.63	4.15
T. M. C	49.0	166	4	3.23	3.94
Average	....	...	..	3.02	3.62

[1] Each experiment consists ordinarily of from 4 to 5 15-minute experimental periods.

COMPARISON OF THE METABOLISM OF THE SAME INDIVIDUAL AS DETERMINED WITH THREE DIFFERENT TYPES OF APPARATUS.

Of the normal subjects studied in this laboratory recently, three of them, F. A. R., J. J. C., and J. R., were experimented upon in all three forms of apparatus, and, therefore, these experiments are especially well designed for comparing the relative metabolism as measured by the three different types of apparatus. This comparison and also a partial comparison with other subjects are made in table 167.

TABLE 167.—*Comparison of the metabolism of normal individuals as determined in different types of apparatus.*

Subject.	Body-weight (without clothing).	Height.	Chair.		Bed.		Respiration apparatus.		Heat per kilo. per hour.	
			Carbon dioxide produced per kilo. per min.	Oxygen consumed per kilo. per min.	Carbon dioxide produced per kilo. per min.	Oxygen consumed per kilo. per min.	Carbon dioxide produced per kilo. per min.	Oxygen consumed per kilo. per min.	Chair.	Bed.
	kilos.	*cms.*	*c. c.*	*c. c.*	*c. c.*	*c. c.*	*c. c.*	*c. c.*	*cals.*	*cals.*
1 F. A. R......	74.4	163	3.27	4.12	2.77	3.34	2.67	3.15	1.17	0.91
2 J. J. C.......	67.6	175	3.29	4.02	2.86	3.36	2.87	3.52	1.34	0.96
3 J. R.	66.0	182	3.47	4.21	2.94	3.59	3.06	3.68	1.20	1.00
Avg. 1 to 3.	....	....	**3.34**	**4.12**	**2.86**	**3.43**	**2.87**	**3.45**	**1.24**	**0.96**
4 T. M. C......	49.0	166	....	....	3.43	4.05	3.23	3.94	....	....
5 F. G. B......	83.0	183	....	....	2.76	3.23	2.67	3.30	....	....
Avg. 1 to 5.	....	....	....	....	**2.95**	**3.51**	**2.90**	**3.52**	....	....
6 L. E. E......	59.6	179	4.20	5.15	....	....	3.63	4.15	....	....

From the values given in table 167, it can be seen that with the three subjects, F. A. R., J. J. C., and J. R., a study can be made of the gaseous exchange as measured with the three different types of apparatus, *i. e.*, the chair calorimeter, the bed calorimeter, and the respiration apparatus, and that the direct heat measurement can be compared on the chair calorimeter and the bed calorimeter. Two other subjects, T. M. C. and F. G. B., were experimented with both in the bed calorimeter and with the respiration apparatus, and, therefore, furnish data for comparing further the carbon-dioxide excretion and oxygen consumption. One other subject, L. E. E., was studied both in the chair calorimeter and with the respiration apparatus, giving additional data for such comparison.

Since in experiments with the bed calorimeter or the respiration apparatus, the subject is lying comfortably on a bed or a couch, one would expect that the gaseous exchange as measured by these two forms of apparatus would be nearly the same. If we consider the average of the subjects, 1 to 3, we find that there are 2.86 c. c. of carbon dioxide per kilogram per minute excreted in the bed calorimeter and 2.87 c. c. on the respiration apparatus. Of oxygen consumed there were 3.43 c. c. with the bed calorimeter and with the respiration apparatus, 3.45 c. c., an agreement that is unusual in physiological experiments. With

subjects, 1 to 5, the agreement is equally as satisfactory, 2.95 c. c. of carbon dioxide eliminated for the bed calorimeter against 2.90 c. c. on the respiration apparatus, and 3.51 c. c. of oxygen consumed with the bed calorimeter against 3.52 c. c. on the respiration apparatus.

A comparison of the results obtained with the chair calorimeter with those obtained either with the bed calorimeter or with the respiration apparatus shows a marked increase when the subject is in the chair calorimeter. This is especially noticeable in the measurement of the heat-elimination, which gives an average of 1.24 calories per kilogram per hour in the chair calorimeter against 0.96 calories per kilogram per hour in the bed calorimeter.

The unusually high gaseous exchange of L. E. E., measured both in the chair calorimeter and on the respiration apparatus, is worthy of note. This subject, with whom a number of experiments have been made, has an unusually high metabolism, as will be seen from tables 164, 166, and 167, and it is a good instance of the marked variations in metabolism that may occasionally be found with normal subjects.

COMPARISON OF METABOLISM MEASUREMENTS WITH THREE DIFFERENT TYPES OF APPARATUS.

The results obtained with the three forms of apparatus with normal subjects are summarized in table 168*a*. For more convenient comparison with data presented in various ways by other investigators, the results given in table 168*a* for the chair and bed calorimeters have been calculated on the basis of per kilogram per hour and per 24 hours, and also for an individual weighing 70 kilograms, and are given in table 168*b*. A general inspection of table 168*a* shows that the average values found with the chair calorimeter are somewhat higher than those with either the bed calorimeter or the respiration apparatus, but it is evident that such a comparison is open to the criticism that a different number of individuals were used in each grouping, and the well-known wide variation in metabolism found with normal individuals, even on the basis of per kilogram of body-weight, may account for any discrepancies observed here.

TABLE 168*a*.—*Comparison of metabolism measurements with three different forms of apparatus.*

Apparatus used.	Per kilo. of body-weight per minute.		Calories per kilo. per hour.
	Carbon dioxide eliminated.	Oxygen consumed.	
	c. c.	*c. c.*	
Chair calorimeter	3.26	3.99	1.21
Bed calorimeter	2.95	3.51	1.01
Respiration apparatus	3.02	3.62	....

TABLE 168*b*.—*Results calculated on the basis of per hour and per 24 hours for 1 kilogram and for 70 kilograms.*

Basis of calculation.	Chair calorimeter.					Bed calorimeter.				
	Carbon dioxide eliminated.		Oxygen absorbed.		Heat eliminated.	Carbon dioxide eliminated.		Oxygen absorbed.		Heat eliminated.
	c. c.	*gms.*	*c. c.*	*gms.*	*cals.*	*c. c.*	*gms.*	*c. c.*	*gms.*	*cals.*
Per kilogram of body-weight per hour	196.0	0.38	239.0	0.34	1.21	177.0	0.35	211.0	0.30	1.01
Per kilogram of body-weight per 24 hours	4694.0	9.22	5740.0	8.20	29.0	4248.0	8.35	5050.0	7.26	24.0
For 70 kilograms per hour	[1]13.7	26.9	[1]16.7	23.9	84.0	[1]12.4	24.4	[1]14.7	21.0	70.0
For 70 kilograms per 24 hours	[1]326.0	645.0	[1]402.0	574.0	2033.0	[1]295.0	585.0	[1]353.0	504.0	1697.0

[1] Liters.

The relationship existing between the metabolism as measured by the three different types of apparatus is best illustrated by a percentage table (table 169) in which the values found in the bed calorimeter are taken on the basis of 100. This table is designed for use in connection with table 168*a*, and shows clearly that the metabolism as measured by the carbon-dioxide production and oxygen consumption is identically the same with both the bed calorimeter and respiration apparatus. With the chair calorimeter, the carbon-dioxide production is 17 per cent higher than with the bed calorimeter, the oxygen absorption 20 per cent, and the heat-elimination 29 per cent. It is of interest to note that with subject 6, who had the abnormally high metabolism, these proportions hold good, relatively speaking. In general, then, we may state that the metabolism as measured in the chair calorimeter is some 20 to 30 per cent greater than with the bed calorimeter or with the respiration apparatus. On the other hand, the results as found by the bed calorimeter and respiration apparatus agree remarkably well.

As the result of a large number of experiments on individuals lying asleep and sitting up in a chair, Benedict and Carpenter[1] concluded that there was an increase in the resting metabolism when a person is sitting up over that when

TABLE 169.—*Percentage comparison of metabolism of normal individuals in chair and bed calorimeters and with the respiration apparatus.*

[Bed = 100 per cent.]

Subjects.	Carbon dioxide eliminated.[1]			Oxygen absorbed.[2]			Heat eliminated.	
	Chair calorimeter.	Bed calorimeter.	Respiration apparatus.	Chair calorimeter.	Bed calorimeter.	Respiration apparatus.	Chair calorimeter.	Bed calorimeter.
1 to 3	117	100	100	120	100	101	129	100
1 to 5	....	100	98	....	100	100	....	....

[1] With subject 6, carbon dioxide with respiration apparatus = 100; with chair = 116.
[2] With subject 6, oxygen with respiration apparatus = 100; with chair = 124.

[1] Benedict and Carpenter, Publication No. 126, Carnegie Institution of Washington, 1910, p. 95.

sleeping, amounting to 46 per cent in the carbon-dioxide production, 29 per cent in the oxygen consumption, and 37 per cent in the heat-elimination. It must be borne in mind, however, that these conclusions were based upon experiments in which there was much greater activity during the period when the subject was sitting up and awake than in the experiments with the new respiration calorimeters. In these latter experiments the subject did not at any time leave the chair and maintained the greatest degree of rest, while in the earlier experiments they occasionally stood up, moved to the food aperture of the calorimeter and returned. Accordingly there was without doubt much greater minor muscular activity and the increased metabolism noted in the earlier experiments would naturally be expected. When we take into consideration this greater muscular activity, therefore, the results found in the earlier experiments with a very much larger number of individuals confirm us in the belief that the values here expressed indicate an increase in metabolism of a subject when sitting in a chair and awake over that when lying asleep, varying from 20 to 30 per cent.

At first sight it may seem somewhat incongruous that the increments in the oxygen consumption and the heat-elimination are not alike, as the difference between the calorimetry as directly measured and the indirect calorimetry computed from the oxygen would apparently indicate an error. As a matter of fact, the agreement between the direct and indirect calorimetry is the subject of a subsequent discussion in this report.[1] The values here found, however, may be of actual use in comparing experiments made with subjects in the sitting posture with those made when the subject is lying on a couch or in bed.

THE GASEOUS EXCHANGE AND ENERGY TRANSFORMATIONS IN DIABETES.

CARBON-DIOXIDE ELIMINATION.

With normal individuals the method of determining the total energy transformations by the measurement of the carbon-dioxide elimination has led to a number of erroneous results, but with diabetics, since the metabolism is largely of fat, this method gives obviously much more accurate results, and consequently the measurements of the carbon-dioxide elimination when accurately made may serve in severe cases of diabetes as a relatively exact indication of the metabolism from day to day. If, on the other hand, the cases of diabetes are such that there is any considerable tolerance for carbohydrate and the metabolism on any given day is in large proportion due to carbohydrate, the use of the carbon-dioxide elimination as an index of the energy metabolism is obviously erroneous.

The data regarding the volume of carbon dioxide eliminated per kilogram of body-weight per minute in the experiments with diabetics here reported have been collected in table 170. All the values given are those for the period 12 hours after the last meal, and hence are probably uninfluenced by the digestive processes. Since the muscular activity varied in the different experiments, the

[1] See p. 188.

results have been grouped under three heads, (1) experiments made with the chair calorimeter when the patients were sitting upright in the chair; (2) those made with the bed calorimeter when the subject was lying on a bed; and (3) those made with the respiration apparatus when the subjects were lying on a couch. While in the presentation of the statistics of each subject certain inferences have been drawn and points emphasized with regard to the katabolism of different individuals on different days, this table shows very clearly the variations in experiments with the same individual.

TABLE 170.—*Carbon dioxide eliminated per kilogram of body-weight per minute by diabetics in experiments without food.*

Subject.	Chair calorimeter.		Bed calorimeter.		Respiration apparatus.	
	Carbon dioxide eliminated.	Average.	Carbon dioxide eliminated.	Average.	Carbon dioxide eliminated.	Average.
Severe diabetes.		c. c.		c. c.		c. c.
Case A	3.38 3.05 3.25 3.37 3.52 3.20 3.43 3.03 3.29	3.28	3.22	3.22	....	....
B	....	....	3.23	3.23	3.04 2.99 2.99 3.17	3.05
C	3.15 3.22 3.14 3.22 3.15 3.03 3.14 3.24	3.16	2.95	2.95	2.79 2.78 2.89 2.60 2.82 2.78 3.33 3.04 3.21 2.92 2.83 2.85 2.87	2.90
D	....	....	....	....	3.25 3.08 3.00	3.11
E	3.40 3.18	3.29	....	....	....	....
F	3.44	3.44	....	....	....	....
G	....	....	3.22	3.22	....	....
H	....	....	3.24 3.08 2.94 3.14 3.19	3.12	3.04	3.04
I	4.32 4.31	4.32	....	....	....	....
J	3.72	3.72	....	....	4.02 3.96 3.48	3.82
Av. of severe cases.	....	3.53	....	3.15	....	3.18
Light diabetes.						
Case K	3.10	3.10	....	....	2.84	2.84
L	3.53 3.42 3.46 3.42	3.46	3.44	3.44	....	....
M	2.41 2.32	2.37	2.57	2.57	....	....
Av. of light cases	....	2.98	....	3.00	....	2.84
Av. of all cases	....	3.35	....	3.11	....	3.13

Considering the experiments with the chair calorimeter it can be seen that with Cases A and C, with whom the larger number of experiments were made, the variations from the average are relatively unimportant. With Case A the range is from 3.03 c. c. to 3.52 c. c., the average being 3.28 c. c. With Case C the range is much less, from 3.03 c. c. to 3.24 c. c., the average being 3.16 c. c. In none of the experiments are there wide ranges between different experiments with the same individual. When it is considered that these experiments were made at many different times during the year and at different stages of the disease, and, indeed, were frequently preceded by a different diet, the uniformity in the results of the determinations of the carbon-dioxide elimination are certainly striking, indicating that the nature of the katabolism must be practically the same throughout the whole period in which each subject was investigated.

Fewer experiments were made with the bed calorimeter, and with but one subject was more than one experiment made with this apparatus, *i. e.,* Case H. These experiments followed each other and hence the range is very small, being from 2.94 c. c. to 3.24 c. c., the average being 3.12 c. c.

With the respiration apparatus we have a large number of experiments, particularly with Case C. These values again show a striking uniformity; the variations are, however, larger than with the chair calorimeter. Thus, with Case C, the variations run from 2.60 c. c. in experiment No. C 15, which is evidently an exceptional experiment, to 3.33 c. c. in experiment No. C 19, the average of all experiments being 2.90 c. c. Here, again, the experiments covered a period of several months, and when the subject was in widely different conditions with regard to his general body-state.

On the whole, the results for carbon dioxide are wonderfully constant considering the possibilities and the nature of the material katabolized at different times of the year and at different stages of disease. This is, however, obviously due to the fact that the metabolism with diabetics is in large part of fat, and carbohydrate plays a relatively unimportant rôle in the total metabolism.

The values also indicate that the muscular activity must have been relatively the same in practically all of the experiments. In the chair calorimeter the subjects were all supposed to be sitting quietly in the chair, reading, and they were requested not to leave the chair or move about unduly. In the bed calorimeter they were lying quietly on a couch inside the chamber, and in many instances were asleep. In the respiration experiments on the couch there was, usually, enforced muscular quiet, as the subjects were not even permitted to turn over or lie on the side, as frequently occurred in the bed calorimeter.

In comparing experiments made under different physical conditions, it is almost impossible to eliminate the variations in muscular activity. On the other hand, with the two calorimeters and the respiration apparatus used in these experiments, it is possible, by means of a series of experiments on the same apparatus with the same subject, to obtain some definite idea with regard to the variations in the total metabolism resulting from a change in position from the couch used with the respiration apparatus and the bed in the bed calorimeter to the sitting position in the chair calorimeter. A discussion of this variation will be found on page 175. From the results given in table 170, it can be seen that the carbon-dioxide excretion per kilogram per minute with different individuals is essentially the same in the bed calorimeter as with the respiration apparatus, but there is a noticeable increase in the carbon-dioxide elimination of subjects in the chair calorimeter—an increase amounting to approximately 8 per cent. The average production of carbon dioxide in cubic centimeters per minute and per kilogram of body-weight was 3.35 c. c. in the chair calorimeter, in the bed calorimeter 3. 11 c. c., and in the respiration experiments 3.13 c. c.

COMPARISON WITH CARBON-DIOXIDE ELIMINATION IN EARLIER EXPERIMENTS WITH DIABETICS.

While the experiments with the chair calorimeter are not strictly comparable with those in which the bed calorimeter and respiration apparatus were used, nevertheless such experiments are extremely interesting in that they can be compared with the work of earlier investigators, many of whom used a respiration chamber or special mouth-breathing appliances, such as the Zuntz-Geppert apparatus.

Of the earlier experiments in which the respiration chamber was used, practically all of the results were obtained when the subject had had food during the experiment or immediately prior thereto. The results obtained with all the cases of diabetes which have been studied in respiration chambers with which we are familiar are collected in table 171, including one experiment of Pettenkofer and Voit with a subject without food and the four experiments of Johansson, in which the subjects were also without food. Food was given in all the other experiments included in the table, although it should be pointed out that the third experiment of Weintraud and Laves approximated those experiments

TABLE 171.—*Carbon dioxide eliminated per kilogram per minute in experiments with food*[1] *in the respiration chamber.*

Experimenter.	Subject.	Age.	Body-weight.	Carbon dioxide elimination per kilo. per minute.	Remarks.
		yrs.	*kilos.*	*c. c.*	
Pettenkofer and Voit (1866)..	Man	21	54.5	[1]3.26	Without food.
			55.0	5.11	Very liberal diet.
			54.5	4.03	Average diet.
			53.0	4.12	Protein-free diet.
			52.0	4.27	Protein-rich diet, no carbohydrates.
			52.0	4.48	Mixed diet.
			51.0	4.58	Do.
Livierato (1888-1889)	Man	40	52.0	3.26	Rich protein diet.
			50.5	3.49	Do.
			51.7	4.91	Do.
			51.6	4.39	Do.
	Woman .	60	39.7	2.99	Do.
			....	3.11	Do.
			....	3.02	Do.
	Girl	19	44.2	3.22	Ordinary diet.
			44.8	3.41	Protein rich diet.
			45.7	3.35	Same one month later.
			48.8	3.31	Do.
Weintraud and Laves (1894)..	Man	27	64.0	4.43	
			....	3.80	Food just before the experiment.
			....	3.65	Five hours after food; asleep.
			....	3.90	Food with levulose.
			....	4.11	Large amounts of bread; urine sugar-free after end of experiment.
Ebstein (1898)	Man		62.5	3.99	
			....	3.79	
Johansson[1] (1908)	Man		61.8	2.62	Without food.
	Man		85.0	2.43	Do.
	Woman .		43.4	3.15	Do.
	Woman .		54.4	2.92	Do.
Dubois and Veeder (1910).....	Man		70.4	3.75	Severe case.
	Man		68.0	4.04	Mild case.

[1] The first experiment reported from the work of Pettenkofer and Voit and the experiments of Johansson were without food

on normal individuals summarized by Benedict and Carpenter,[1] in which the metabolism was determined from 1 a. m. to 7 a. m. The subject in this experiment had been without food 5 hours, and for the greater part of the experiment was asleep. The influence of the ingestion of food is markedly shown in the experiments reported by Pettenkofer and Voit, and also with the subject of Weintraud and Laves.

While the majority of these earlier experiments with the respiration chamber have been made with subjects during digestion or with food, most of the experiments with the Zuntz-Geppert respiration apparatus were made 12 hours after the last meal, although certain investigators used this apparatus in studying the influence of the ingestion of food on the metabolism. Fortunately, most of the investigators have been pupils of Zuntz, and were well trained in his technique, and therefore the results are extremely reliable. The carbon-dioxide eliminations per kilogram of body-weight in experiments without food in which the Zuntz-Geppert apparatus has been used have been brought together and placed in table 172. The variations found with different individuals in the amounts of carbon dioxide eliminated are indeed striking, ranging from as low as 2.04 c. c. to 4.80 c. c. There is likewise a wide range in the age and body-weight of the different subjects, the lowest values being found with fat individuals and the highest with a young boy, weighing but 35 kilograms and 11 years of age.

In considering the researches of earlier investigators it is necessary for us to take into consideration the muscular activity of the subject. In all of the respiration experiments, excepting those of Johansson, we deal with a condition of body activity that is unquestionably somewhat greater than in the experiments with the Zuntz-Geppert respiration apparatus, where the subjects lay quietly with enforced muscular rest on a couch. In the data for the earlier experiments we find too little evidence with regard to the muscular activity, particularly in the early experiments of Livierato, and Pettenkofer and Voit. In the experiments of Weintraud and Laves the subjects sat quietly in a chair, and therefore the muscular activity must have been not far from that in the experiments here reported made with the chair calorimeter. On the other hand, in the experiments of Ebstein and of Dubois and Veeder, there was in all probability more muscular activity during the period.

Unfortunately with the uncertain amount of muscular activity in many of the earlier experiments, it is difficult to draw a sharp line between the values obtained while resting on the couch and those obtained inside of the respiration chamber. Unquestionably, from the experiments of Weintraud and Laves, where the subject sat practically all the night sleeping in a chair, the results are nearer to those obtained with the bed calorimeter or with the subject lying on a couch than any others aside from those made by Johansson when the sub-

[1] Benedict and Carpenter, Carnegie Institution of Washington, Publication No. 126, 1910.

ject was trained to control the body with unusual muscular quietness and rest. The differences in muscular activity, in the state of digestion, and in the methods employed make a strict comparison somewhat difficult, and the results given by these early investigators are here tabulated only to give a general resumé of the early researches on diabetes in the special field of carbon-dioxide elimination and oxygen absorption.

TABLE 172.—*Carbon dioxide eliminated per kilogram per minute in experiments without food as determined by the Zuntz-Geppert respiration apparatus.*

Experimenter.	Subject.	Age.	Body-weight.	Carbon dioxide elimination per kilo. per minute.	Remarks.
		yrs.	*kilos.*	*c. c.*	
Leo (1891)	Man	51	55	3.21	Severe diabetes; Magnus-Levy says moderately light.
	Man	52	75	2.88	Light diabetes.
	Man	47	90.5	2.31	Light diabetes (fat).
	Man	39	63	2.80	Light diabetes.
	Man	45	72	2.84	Severe case.
Stüve (1896)	Case I	(?)	(?)	2.93	(?)
	Case II	(?)	(?)	2.93	Urine sugar-free.
			....	3.06	Sugar in urine.
Nehring and Schmoll (1897)	Boy	15	57.5	3.41	Moderately severe case of diabetes.
			....	3.12	
			....	3.45	
			....	3.90	
			....	3.27	
			....	3.33	
	Woman (?)		74	2.51	Do.
			....	2.62	
Magnus-Levy (1905)	Man	43	62.2	3.25	Severe case.
			....	2.94	
			....	3.27	
			....	3.56	
			....	3.05	
			....	3.26	
			....	3.44	
			....	3.17	
			....	3.38	
			....	3.01	
	Woman	35	33.8	3.66	Severe.
			....	3.96	
			....	3.66	
			....	3.64	
	Man	40	44.4	3.74	
	Man	71	91.5	2.04	
	Woman	69	58.6	2.71	
			....	2.65	
			....	2.77	
	Woman	56	54.5	3.03	
Mohr (1907)	Woman	52	84.5	2.22	
			....	2.44	
			....	2.22	
	Boy	11	35	4.55	
			....	4.64	
			....	4.80	
			....	4.75	
			....	4.67	

OXYGEN ABSORPTION.

While the determination of the carbon-dioxide elimination in cases of diabetes is not extremely difficult, the direct determination of the oxygen consumption, especially in a chamber apparatus, is very difficult, and has heretofore not been attempted, save in the experiments of Weintraud and Laves. Pettenkofer and Voit did attempt to determine the oxygen consumption indirectly, but this

has been the subject of much criticism, as will be seen on page 6. In the experiments here reported with both calorimeters and with the respiration apparatus, oxygen was determined directly.

The direct determination of the oxygen consumption of man has a much greater value as a rule than the determination of the carbon-dioxide elimination, since the relation between the oxygen consumption and the heat-elimination is much more constant than between the carbon-dioxide production and the heat-elimination, and thus it has been possible in instances where the direct heat measurements are lacking to compute indirectly the heat from the determination of the oxygen consumption. Hence, in the more recent experiments on diabetes, the determination of the oxygen consumption has been accorded special attention, since the chamber apparatus had been so perfected that accurate direct determinations of the oxygen consumption could be made. The values found in the different cases are presented in table 173.

TABLE 173.—*Oxygen absorbed per kilogram of body-weight per minute in experiments with diabetics without food.*

Subject.	Chair calorimeter.		Bed calorimeter.		Respiration apparatus.	
	Oxygen absorbed.	Average.	Oxygen absorbed.	Average.	Oxygen absorbed.	Average.
Severe diabetes.		*c. c.*		*c. c.*		*c. c.*
Case A	4.86 4.34 4.38 4.92 4.86 4.50 5.17 4.13 4.44	4.62	4.22	4.22	....	....
B	....	....	4.42	4.42	4.27 4.04 4.31 4.47	4.27
C	4.20 4.31 4.72 4.80 4.55 4.08 4.40 4.54	4.45	4.15	4.15	4.01 4.44 4.08 3.82 4.23 3.93 4.85 4.28 4.52 4.44 4.19 4.06 4.14	4.23
D	....	....	....	....	4.44 4.14 4.00	4.19
E	4.73 4.32	4.53	....	....	....	....
F	4.66	4.66	....	....	....	....
G	....	....	4.38	4.38	....	....
H	....	....	4.34 3.88 3.63 4.32 4.17	4.07	4.03	4.03
I	5.65 5.98	5.82	....	....	....	....
J	5.01	5.01	....	....	....	....
Av. of severe cases.	....	*4.85*	....	*4.25*	....	*4.18*
Light diabetes.						
Case K	4.06	4.06	....	....	4.04	4.04
L	4.55 4.58 4.64 4.35	4.53	4.41	4.41	....	....
M	3.09 3.20	3.15	3.28	3.28	....	...
Av. of light cases	....	*3.91*	....	*3.85*	....	*4.04*
Av. of all cases	....	**4.54**	....	**4.13**	....	**4.15**

It is here to be remembered that each experiment with the chair calorimeter may consist of three to six 1- or 2-hour periods, and that each experiment with the respiration apparatus usually consists of three to five 15-minute periods. The variation in the values found for the oxygen consumption of different subjects is somewhat larger than that found for carbon-dioxide elimination. Thus, with Case A, the variations are from 4.13 c. c. to 5.17 c. c., the average for all

being 4.62 c. c. With Case C the variations ranged from 4.08 c. c. to 4.80 c. c., and the average was 4.45 c. c. These values are fully in accord with those found in experiments with the respiration apparatus where, with Case C, the variations ranged from 3.82 c. c. to 4.85 c. c. The extremely high value of 5.82 c. c. was with the greatly emaciated subject I, while the lowest values, 3.09 c. c. and 3.20 c. c., were with the fat man with light diabetes. On the whole, however the agreement between different experiments with the same subject is all that could be desired. As with the measurements of carbon-dioxide elimination, it is seen here that the highest amount found on the average in all experiments with all subjects is found with the chair calorimeter, *i. e.*, 4.54 c. c., and the values for the experiments in the bed calorimeter and with the respiration apparatus are considerably lower.

COMPARISON WITH OXYGEN ABSORPTION IN EARLIER EXPERIMENTS WITH DIABETICS.

The results here given can be compared with those given by earlier writers only in so far as the earlier experiments were made with the Zuntz-Geppert apparatus, with the single exception of the experiments of Johansson, for unquestionably the experiments with the larger chamber, aside from those of Johansson, include much greater muscular activity than was exhibited by the subjects of these experiments, excepting, possibly, experiment No. 3 of Weintraud and Laves.

In these earlier experiments the only determinations of the oxygen consumption of diabetics inside of the respiration chamber are those made by Weintraud and Laves in 1894. With a subject 27 years of age and weighing 64 kilograms, they found in five experiments, ranging from 9 to 10 hours each, an oxygen consumption per kilogram per minute of 6.23, 6.16, 5.74, 5.59, and 5.53 c. c., respectively. Just before the second experiment, food had been taken. The third experiment was made 5 hours after the last meal and the subject was for the most part asleep. Food was taken in the fourth experiment, and with it a large amount of levulose; in the last experiment considerable amounts of bread were taken. As a matter of fact, at the end of this last experiment the urine was sugar-free.

With the Zuntz-Geppert apparatus, on the other hand, in practically all of the experiments where the carbon-dioxide elimination was determined, the oxygen consumption was also determined, and unusual emphasis is laid on the determination of the consumption of oxygen owing to its being a better criterion of the energy transformations. The values obtained by different investigators for different cases of diabetes are given in table 174. The variations in the physical characteristics, sex, age, and body-weight, are here very noticeable, the largest amounts of oxygen consumed per kilogram of body-weight being found with the 11-year old boy of Mohr, and the smallest amounts with the fat men of Leo and of Magnus-Levy.

TABLE 174.—*Oxygen absorbed per kilogram of body-weight per minute in experiments without food as determined with the Zuntz-Geppert respiration apparatus.*

Experimenter.	Subject.	Age.	Body-weight.	Oxygen consumed per kilo. of body-weight per minute.	Remarks.
		yrs.	*kilos.*	*c. c.*	
Leo (1891)	Man	51	55	4.01	Severe diabetes; Magnus-Levy says moderately light.
	Man	52	75	3.87	Light diabetes.
	Man	47	90.5	2.84	Light diabetes (fat).
	Man	39	63	3.48	Light diabetes.
	Man	45	72	4.77	Severe case.
Stüve (1896)	Case I	(?)	(?)	4.04	(?)
	Case II	(?)	(?)	3.96	Urine sugar-free.
			....	4.13	Sugar in urine.
Nehring and Schmoll (1897)	Boy	15	57.5	4.50	Moderately severe case of diabetes.
			....	4.20	
			....	4.56	
			....	4.71	
			....	4.64	
			....	4.25	
	Woman (?)		74	3.68	Do.
			....	3.73	
Magnus-Levy (1905?)	Man	43	62.2	4.97	Severe case.
			....	4.47	
			....	4.70	
			....	4.53	
			....	4.69	
			....	4.44	
			....	4.88	
			....	4.73	
			....	4.84	
			....	4.45	
	Woman	35	33.8	5.04	Severe.
			....	5.54	
			....	4.98	
			....	5.22	
	Man	40	44.4	5.88	
	Man	71	91.5	2.82	
	Woman	69	58.6	3.94	
			....	3.75	
			....	3.96	
Mohr (1907)	Woman	56	54.5	4.73	
	Woman	52	84.5	3.14	
			....	3.20	
			....	3.14	
	Boy	11	35	6.58	
			....	6.24	
			....	6.38	
			....	6.58	
			....	6.63	

It is obvious, from a consideration of a table such as this, that the individual differences in the oxygen consumption per kilogram of body-weight per minute may vary widely. We deal with several factors, all of which may influence more or less the oxygen consumption, such as the age, body-weight, and the severity of the diabetes, and particularly the degree of emaciation to which the subject has been brought in the course of the disease. Under these conditions, therefore, it is seen that the most rigid system of normal controls must be applied before proper deductions can be drawn in regard to the oxygen consumption of diabetics when compared with normal men.

COMPARISON OF THE GASEOUS EXCHANGE OF DIABETICS AS DETERMINED WITH THREE DIFFERENT TYPES OF APPARATUS.

CARBON-DIOXIDE ELIMINATION.

Of the greatest importance is the comparison of the metabolism under the different conditions of body-activity obtaining in these experiments. The larger number of experiments, as has been stated before, were made either with the chair calorimeter or with the respiration apparatus when the subject was lying on a couch. A few experiments were also made with the bed calorimeter. It is of importance, therefore, to note the average differences in the metabolism resulting from these varying body-positions and conditions of experimenting. It so happens that we have four cases who were experimented on in both the chair calorimeter and in the bed calorimeter, three cases in the chair calorimeter and with the respiration apparatus, and one case in both the bed calorimeter and the respiration apparatus, while experiments with Case C were made with all three forms of apparatus. The results for the different subjects whose metabolism can be compared have been brought together in table 175 to show the elimination of carbon dioxide.

TABLE 175.—*Comparison of carbon dioxide eliminated per kilogram of body-weight per minute in experiments with diabetics without food.*

[Average amounts.]

Subject.	Chair calorimeter.		Bed calorimeter.		Respiration apparatus.	
	Number of periods.	Carbon dioxide eliminated.	Number of periods.	Carbon dioxide eliminated.	Number of periods.	Carbon dioxide eliminated.
		c. c.		c. c.		c. c.
Case A	37	3.28	5	3.22	....	....
C	25	3.16	2	2.95	....	....
L	21	3.46	6	3.44	....	....
M	7	2.37	3	2.57	....	....
Average	....	3.07	....	3.04	....	....
Case C	25	3.16	....	....	53	2.90
J	3	3.72	....	....	9	3.82
K	4	3.10	....	....	5	2.84
Average	....	3.33	....	....	....	3.19
Case B	....	....	3	3.23	17	3.05
H	....	....	13	3.12	3	3.04

All the subjects with whom experiments were made in both the chair and bed calorimeters had a slightly larger carbon-dioxide production with the chair calorimeter than with the bed calorimeter. Unfortunately, there are no cases in which experiments with both forms of apparatus included a large number of periods. For instance, with Case A we have 37 hours inside the chair calorimeter but only five periods (total of 3 hours) in the bed calorimeter, and

with Case C we have 25 hours in the chair calorimeter and but 2 hours in the bed calorimeter. Case L showed practically no difference between the two forms of apparatus, and Case M showed an actually larger carbon-dioxide production with the bed calorimeter. It should be said, however, that Case M was the lightest case of diabetes, and he had quite a considerable carbohydrate tolerance, which might account for the larger carbon-dioxide excretion during this period. Furthermore, both Case L and Case M found the sojourn in the bed calorimeter much more trying than in the chair calorimeter. One of the primary purposes of constructing the bed calorimeter was to provide an apparatus in which the subjects could lie for a considerable length of time comfortably, and, indeed, go to sleep if they desired. Case L was a nervous individual who did not find the sojourn in the chamber comfortable, and Case M, who was a large man, also found difficulty in moving about in the narrow confines of the chamber and was rather uncomfortable. It is evident, therefore, that the comparisons here made are by no means satisfactory, first, because the number of experiments made with the different subjects is not the same with the two forms of apparatus; and, second, in those instances where the larger number of experiments was made with the bed calorimeter, the subjects were particularly uncomfortable inside the chamber.

When we compare the experiments made with the chair calorimeter and with the respiration apparatus, we find we have one case which gives a very satisfactory comparison. Case C had 25 periods with the chair calorimeter and 53 periods with the respiration apparatus on the couch. Under these conditions, therefore, we have a sufficient number of periods for a satisfactory basis of comparison.

Case J was a high-strung, nervous individual, who was extremely apprehensive, and whose first introduction to the laboratory was in connection with some experiments on the couch connected with the respiration apparatus. He was so nervous that it was practically impossible to conduct satisfactory respiration experiments with him. The results of three 1-hour periods in the chair calorimeter are also given in the table.

Case K, who was the subject of a limited number of experiments, both in the chair calorimeter and with the respiration apparatus, was a very satisfactory subject, and in all probability the differences in the carbon-dioxide excretion indicate in a general way the differences in metabolism with this individual.

Averaging the results with the three individuals, we find a somewhat lessened metabolism with the respiration apparatus over that in the chair calorimeter. Discarding the results of Case J, we find a noticeably decreased metabolism when the above comparison is made.

Three subjects permit of a comparison between the bed calorimeter and the respiration apparatus. Case C had two periods in the bed calorimeter and 53 periods with the respiration apparatus; case H had 13 periods in the bed calorimeter and three periods on the respiration apparatus, while Case B had

three periods in the bed calorimeter and 17 periods with the respiration apparatus. It is interesting to note that aside from Case B there is practically the same metabolism in both kinds of experiments.

It is clear from these experiments that in general there is not a noticeable difference between the metabolism measured on the couch with the respiration apparatus and in the bed calorimeter. On the other hand, in the experiments which can best be compared, it is obvious that there is a noticeable increase in the values obtained with the chair calorimeter over those with the bed calorimeter and the respiration apparatus. Both of these findings are in full harmony with similar comparisons made with experiments on normal subjects in which the three different forms of apparatus were used.

OXYGEN ABSORPTION.

The values for the oxygen absorption as found with three different types of apparatus are given in table 176. The points raised in connection with the question of the carbon-dioxide comparison obtain with almost equal value in the instances here reported. Thus, with Case M, there is a somewhat larger oxygen consumption in the bed calorimeter than in the chair calorimeter, while the increased metabolism as measured by the carbon-dioxide production of Case K in the chair calorimeter is not noted when the oxygen measurement is taken into consideration with the same subject. Again, comparisons between those experiments which were made with the bed calorimeter and with the respiration apparatus indicate that the metabolism is essentially the same when measured with either type of apparatus.

TABLE 176.—*Comparison of oxygen absorbed per kilogram of body-weight per minute in experiments with diabetics without food.*

[Average amounts.]

Subject.	Chair calorimeter.		Bed calorimeter.		Respiration apparatus.	
	Number of periods.	Oxygen absorbed.	Number of periods.	Oxygen absorbed.	Number of periods.	Oxygen absorbed.
		c. c.		c. c.		c. c.
Case A	32	4.62	1	4.22	....	....
C	22	4.45	2	4.15	....	....
L	20	4.53	6	4.41	....	....
M	6	3.15	3	3.28	....	....
Average	....	4.19	....	4.02	....	....
Case C	22	4.45	....	....	51	4.23
K	3	4.06	....	....	5	4.04
Average	....	4.26	....	....	....	4.14
Case B	....	....	2	4.42	12	4.27
H	....	....	13	4.07	3	4.03

THE ENERGY TRANSFORMATIONS OF DIABETICS.

INDIRECT CALORIMETRY.

As a result of the fundamental researches of Rubner and of Zuntz and his associates, it is possible to compute from the gaseous exchange the approximate heat-production of man in 24 hours, and until now this has been the only method available for obtaining this value. Heretofore, from the carbon-dioxide determinations alone, it has been impossible to more than roughly approximate the energy transformations in a day, and the more accurate estimates of this value have been those which were based upon the determination of the oxygen consumed. When the elimination of carbon dioxide, the oxygen consumption, and the nitrogen excretion are accurately known, the computation of the energy transformation is most satisfactory for 24-hour experiments. Such computations from the gaseous exchange have frequently been compared with the direct determination of the energy transformation by the respiration calorimeter, and for periods of 24 hours or more the agreement has been all that could be desired.

It is impracticable here to enter into a lengthy discussion of the accuracy of the methods of indirect calorimetry when applied to short periods. These methods are now undergoing rigid tests at the Nutrition Laboratory, and strict comparison is being made of the results obtained by direct and indirect calorimetry. With healthy individuals in a state of fast it is not difficult to make a very satisfactory computation of the energy transformation from the gaseous exchange, but the problem becomes somewhat more complicated when food is given, especially nitrogenous food. Various methods have been devised for computing the energy transformations in short periods, and these have been used in a number of experiments, particularly on animals, but all the methods have been based upon the original data of Zuntz and his co-workers.

An attempt has been made by many investigators to use the indirect method for computing the energy transformation from the gaseous exchange in studying the metabolism of diabetics. With diabetics, however, not only the unburned nitrogenous material from protein, but also sugar from either preformed sugar in the body or from sugar formed from protein is excreted in the urine, and the calculations are accordingly more complicated.

From the 24-hour experiments of Pettenkofer and Voit, Ebstein, and Weintraud and Laves, Magnus-Levy has computed the energy transformations per 24 hours in each of the three studies to have been 36, 36, and 37 calories, respectively, per kilogram of body-weight and per 24 hours. In the experiments of Weintraud and Laves, Magnus-Levy used the carbon-dioxide values rather than those for oxygen absorption, as they seemed to be more accurate. Dubois and Veeder have calculated that the energy transformations in the studies made by them were 34.3 calories per 24 hours per kilogram of body-weight with the severe cases of diabetes, and 31.7 calories with the cases of mild diabetes.

Direct Calorimetry.

In the experiments on diabetics here reported the energy transformations were directly measured by means of the two respiration calorimeters. A part of the heat eliminated was absorbed and brought away by a water-current flowing through the chamber, and a part was used to vaporize the water in the air. The accuracy of the apparatus for the measurement of the heat-elimination has been discussed in detail in another place.[1]

An attempt was made in these studies to shorten the experimental period to 1 hour, and, indeed, the heat-production has frequently been computed on the basis of 1 hour; nevertheless, for final conclusions we must use the heat-production for the total experimental period inside the respiration chamber, and thus eliminate any minor errors due to the apportionment of the heat-measurement over as short a period as 1 hour.

The difficulties of distinguishing clearly between the heat-production and the heat elimination have already been pointed out,[2] as well as the methods described for securing the body-temperature correction. The measurements of body-temperature which were made in connection with these experiments, while much more accurate than those ordinarily made, are still unsatisfactory for the most accurate apportionment of the heat-measurements between the heat-elimination and heat-production. Fortunately, as the subjects were either lying or sitting quietly throughout the whole period of the experiment, there was doubtless in all cases only minimum temperature alteration. The only experiments in which there was probably any material alteration in the body-temperature, such as would affect the heat-elimination, were those in which food was taken.

The measurements of heat are in large part influenced by the degree of muscular activity of the subject. In these experiments the subjects were all cautioned to remain unusually quiet inside the chamber or lying on the bed and to keep the muscular activity at the lowest possible point. While there were wide variations in muscular activity with different individuals, on the whole the diabetics were extremely quiet throughout the experiments. They did not, of course, maintain the state of complete muscular rest assumed by the subjects of Zuntz or Johansson, but it is to be noted that the experiments of Zuntz rarely lasted more than 20 minutes, while those of Johansson were of necessity restricted to 1 hour in length, as it was impossible for subjects to maintain such enforced muscular rest longer than this period.

As in the experiments with diabetics, particularly in those without food and without muscular activity, the body-temperature did not change materially, it has been considered advisable to use in all calculations the heat-elimination as measured by the calorimeter, without making corrections for the slight variations in body-temperature. With all the subjects it was not possible to use the electrical-resistance thermometer, and with certain subjects the clinical thermom-

[1] Benedict, Riche and Emmes, Am. Journ. Physiol., 1910, 26, p. 1.
[2] See p. 19.

eters were not used with any great degree of satisfaction, since the subject must take the temperature himself inside the chamber. It is hardly probable, however, that in averaging so large a number of experiments, as is frequently the case here, any considerable errors can be introduced by neglecting to take into consideration the heat-production instead of the heat-elimination.

TABLE 177.—*Heat eliminated per kilogram of body-weight per hour and per kilogram per 24 hours in experiments without food.*

Subject.	Chair calorimeter.			Bed calorimeter.		
	Heat eliminated.	Average.	Per kilogram per 24 hours.	Heat eliminated.	Average.	Per kilogram per 24 hours.
Severe diabetes.	*calories.*	*cals.*	*cals.*	*calories.*	*cals.*	*cals.*
Case A	1.43 1.27 1.33 1.50 1.42 1.34 1.41 1.19 1.18	1.34	32.2	1.14	1.14	27.4
B	....	....	....	1.24	1.24	29.8
C	1.28 1.23 1.24 1.28 1.36 1.26 1.40 1.26	1.29	31.0	....	....	....
E	1.38 1.30	1.34	32.2	....	....	....
F	1.39	1.39	33.4	....	....	....
G	....	....	....	1.15	1.15	27.6
H	....	....	....	1.16 0.94 1.05 1.08 1.22	1.09	26.2
I	1.69 1.61	1.65	39.6	....	....	....
J	1.36	1.36	32.6	....	....	....
Av. of severe cases	....	1.40	33.6	....	1.15	27.6
Light diabetes.						
Case K	1.31	1.31	31.4	....	....	....
L	1.30 1.34 1.35 1.37	1.34	32.2	1.29	1.29	31.0
M	1.05 0.90	0.98	23.5	0.99	0.99	23.8
Av. of light cases	....	1.21	29.0	....	1.14	27.4
Av. of all cases	....	1.33	31.9	....	1.15	27.6

A summary of the measurements of the heat-elimination in all the experiments, expressed on the basis of per kilogram of body-weight per hour, has been placed in table 177. With Case A there was an unusually low heat-elimination in the last two experiments with the chair calorimeter, much lower than in any other period. With Case C in the chair calorimeter the results from experiment to experiment are strikingly uniform. The unusually high heat-production of Case I agrees also completely with the unusually high oxygen consumption and carbon-dioxide production shown by this subject. Similarly, the extremely low values found with Case M in both the bed and the chair calorimeters are in accord with the observations of the carbon-dioxide elimination and oxygen consumption. With the bed calorimeter, the observations are more or less fragmentary, usually consisting of but one experiment with each subject. The average heat-elimination of all the subjects in the chair calorimeter is 1.33 calories per kilogram per hour and 1.15 calories with the bed calorimeter. A strict comparison between these two values is not permissible, since a much larger number of experiments was made with the chair calorimeter with a much larger number of subjects.

As was seen in the discussion of the carbon-dioxide production and oxygen absorption, the chair calorimeter usually gave values some 15 to 20 per cent higher than the bed calorimeter. Here, although the basis is unsatisfactory for the best comparison, we still have an increase ranging from 15 to 20 per cent.

It has been the custom of most writers to give the heat-elimination on the basis of per kilogram of body-weight per 24 hours, and a column has therefore been added to the table giving the values in this way. This is, however, somewhat illogical, since it is not at all probable that the metabolism as measured either in the chair calorimeter or in the bed calorimeter is in any way representative of the average metabolism of a 24-hour day. Unquestionably, the subjects while sitting in the chair calorimeter are more active muscularly and have a higher metabolism than when in bed asleep at night, and, on the other hand, while sitting in the chair calorimeter, they would have a lower metabolism than in moving about the house or engaged in any business occupation. It is probable, however, that in view of the general weakened condition of diabetics and their tendency to conserve energy more or less, the values found with the chair calorimeter represent more nearly the actual 24-hour metabolism than any thus far obtained, although no doubt these values are somewhat less than the metabolism outside of the chamber would be when the subjects are free to move about.

COMPARISON OF THE METABOLISM IN DIABETES OF DIFFERENT DEGREES OF SEVERITY.

In all of the tables and discussion thus far presented there are not sufficient data to note material alterations in the metabolism of the same individual at different times of the year or different stages of the disease, with the single exception of the last fasting experiment with Case A, where the metabolism was noticeably lower than in the earlier experiments.[1] Consequently, there has been as yet no means for judging of the influence of varying degrees of severity of the disease upon metabolism.

Considering the experiments in two groups, those of the severe and light cases, it will be of interest to compare the metabolism as measured on these two different groups of individuals. The comparison, however, can be made only with the chair calorimeter, for the experiments in the bed calorimeter, all with light cases, were too few to be of any service, only two experiments, one with Case L and one with Case M, being available. The metabolism as indicated by the carbon-dioxide production and oxygen consumption per kilogram of body-weight per minute, as well as the heat-elimination per kilogram of body-weight per hour, are given in table 178, in which the averages of the severe cases and of the light cases are compared.

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[1] Clinically at this time the patient was in better condition than during the earlier experiments.

TABLE 178.—*Comparison of the metabolism of severe with light diabetes in the chair calorimeter.*

	Cubic centimeters per minute per kilo.		Heat eliminated per kilo. per hour.
	Carbon dioxide.	Oxygen.	
	c. c.	*c. c.*	*calories.*
Severe	3.53	4.85	1.40
Light	2.98	3.91	1.21

The results of this comparison show that the carbon-dioxide production is noticeably higher in the severe cases than with the light cases. This is also indicated by the oxygen consumption and the heat-elimination. The objection may readily be raised with this comparison, however, that of the three light cases, Case M was abnormally fat, and, therefore, had an abnormally low metabolism per kilogram of body-weight. On the other hand, an inspection of the data shows that the metabolism for Case L was unusually high, and probably the average of these three may still represent a fair average of so-called "light" cases of diabetes.

The values found indicate a noticeable increase in the carbon-dioxide production, oxygen consumption, and heat-elimination per kilogram of body-weight with severe cases, when compared with light cases. On the other hand, the results found with Case L indicate that there may be light cases of diabetes which give a high metabolism per kilogram of body-weight, and consequently no value may be expected to be derived from a measurement of the intensity of metabolism as an index of the severity of any case. It is true, however, that practically all of the severe cases have a value higher than the highest value found with the light cases, at least so far as the oxygen consumption is concerned. It is furthermore highly probable that with the same individual the more severe the acidosis the higher the metabolism.

COMPARISON OF THE METABOLISM IN DIABETES WITH METABOLISM IN HEALTH.

Since it was clearly shown in the comparison of the metabolism of individuals with diabetes of different degrees of severity that the more severe the case the greater the metabolism, the comparison of diabetics with normal individuals would, *à priori*, be expected to show a larger metabolism with diabetes than in health. Using for comparison the normal experiments made in this laboratory with the same type of apparatus employed in making the experiments on diabetics, the average results have been brought together in table 179, in which are compared the results with normal individuals, with all the cases of diabetes, and with all the severe cases of diabetes. In order to furnish the best means for comparison, the values are all given on the basis of per kilogram of body-weight per minute, the results for the heat eliminated being presented on the basis of per kilogram of body-weight per hour and per 24 hours.

TABLE 179.—*Comparison of carbon dioxide eliminated, oxygen absorbed, and heat eliminated by diabetics and by normal individuals.*

Subjects.	Carbon dioxide per kilo. of body-weight per minute.			Oxygen per kilo. of body-weight per minute.			Heat. Per kilo. of body-weight per hour.		Heat. Per kilo. of body-weight per 24 hours.	
	Chair.	Bed.	Respiration apparatus.	Chair.	Bed.	Respiration apparatus.	Chair.	Bed.	Chair.	Bed.
	c. c.	*c. c.*	*c. c.*	*c. c.*	*c. c.*	*c. c.*	*cals.*	*cals.*	*cals*	*cals.*
Normal individuals	3.26	2.95	3.02	3.99	3.51	3.62	1.21	1.01	29.0	24.2
Diabetes, all cases	3.35	3.11	3.13	4.54	4.13	4.15	1.33	1.15	31.9	27.6
Diabetes, severe cases	3.53	3.15	3.18	4.85	4.25	4.18	1.40	1.15	33.6	27.6
Percentage increase, severe over normal	8.3	6.8	5.3	21.6	21.1	15.5	15.7	13.9	15.7	13.9

The noticeable increase in the average metabolism of diabetics over normal metabolism is marked in both the oxygen consumption and in the heat-production. The increase in carbon-dioxide elimination, though positive, is much less. At first sight this appears to be a marked discrepancy in the results. On the other hand, the normal individual, even when no food is eaten, has a much larger supply of carbohydrates stored as glycogen that he can draw upon than have diabetics, and the carbon-dioxide excretion of normal individuals would, under otherwise uniform conditions, be expected to be somewhat larger than that of a diabetic subsisting upon a diabetic or flesh-fat diet with a minimum of carbohydrate. We see, therefore, that the positive increase in the carbon-dioxide excretion in diabetes, slight though it may be, is all the more remarkable, and is wholly in harmony with the large increases noted with the oxygen consumption and the heat-production.

The percentage increases have been included and it is seen that the carbon-dioxide excretion averages not far from 6 to 7 per cent, the oxygen consumption from 16 to 21 per cent, and the heat-elimination about 15 per cent. The positive increase measured by all these three factors is such as to leave no doubt that in the diabetic individuals here studied there was a distinct increase in metabolism above normal.

Inasmuch as this finding is distinctly opposed to many commonly accepted beliefs, the experiments must be subjected to a critical examination and study, and all possible influences on the metabolism taken into consideration. The criticisms raised, therefore, in the subsequent sections of this report will deal, first, with the validity of the value assumed as normal, and, second, with all possible factors occurring to the writers that might influence the metabolism of the diabetics which were not present in the normal experiments.

THE NITROGEN AND SUGAR EXCRETIONS OF DIABETICS IN PERIODS WITHOUT FOOD.

THE NITROGEN EXCRETION.

Among the numerous possible explanations of the increased metabolism noted in diabetes may be the inference that there is a larger katabolism of protein with diabetics and that the specific dynamic action of the protein causes the increased metabolism. In order to throw some light upon the relative amount of protein katabolized by these individuals, the calculations have been made showing the nitrogen in the urine per kilogram of body-weight per hour expressed as milligrams for the various fasting experiments. While it was formerly believed that enormous amounts of protein were katabolized by diabetics and enormous amounts of protein were given in the earlier dietetic treatment of diabetes, with the more modern treatment the nitrogen ingested per day is considerably less. It is of interest, therefore, to determine the nitrogen excretion of these different subjects at least 12 hours after the last meal on different days and during different periods of the year. The results are given in table 180.

The differences in the amounts thus excreted are very noticeable. Thus, with Case A, on December 16, 1908, there were but 4.1 milligrams of nitrogen per kilogram per hour in an 8-hour period, while on November 5, 1909, in 3 hours there were 12.5 milligrams, or nearly three times the former amount. The values found with Case C range from 6.3 milligrams to 16 milligrams, and, indeed, these wide variations are found in experiments but 4 days apart. In experiments with Case H, 1 week apart, the nitrogen ranged from 6.3 milligrams to 14.5 milligrams. In most of the other experiments the variations are not so great and the amounts remained relatively uniform. It should be stated, however, that with no other case did the experiments extend over so long a period of time as with Cases A and C. The average values for the different individuals shown in the table range from 5.8 milligrams with Case B to 13.8 milligrams with Case I, the average of all the severe cases being 9.6 milligrams, and the light cases 8.7 milligrams, the average for all cases being 9.4 milligrams.

From these results it is clear that the amount of nitrogen excreted 12 hours after the last meal may vary considerably with the same subject at different times, and likewise between different subjects, although on the average it is not far from 10 milligrams per kilogram of body-weight per hour.

For comparison it is necessary for us to make similar analyses of the urine of normal individuals. This we have done in connection with several of the normal experiments included in this report, and the results are abstracted in table 181.

Of special significance is the fact that the variations between the minimum and the maximum amount for nitrogen per kilogram per hour are very much less with normal individuals than with diabetics, the widest variations being with the subject J. R., ranging from 3.8 milligrams to 8.7 milligrams. The

TABLE 180.—*Nitrogen excretion per kilogram of body-weight in periods without food.*

Date.	Hours.	Milli-grams.	Date.	Hours.	Milli-grams.
Case A.			*Case F.*		
Nov. 4, 1908	7	10.0	Nov. 11, 1908	8	10.0
Nov. 18, 1908	8	6.4			
Dec. 16, 1908	8	4.1	*Case G.*		
Mar. 4, 1909	5	8.5	Feb. 16, 1908	8	8.5
Mar. 13, 1909	4	6.9			
Mar. 19, 1909	6	9.1	*Case H.*		
Mar. 26, 1909	6	7.7	Feb. 1, 1910	5	6.3
May 17, 1909	7	6.8	Feb. 7, 1910	5	7.8
Nov. 5, 1909	3	12.5	Feb. 9, 1910	7	14.5
Mar. 11, 1910	5	7.9	Feb. 12, 1910	6	8.2
			Mar. 5, 1910	7	9.0
Average	..	8.0	Average	..	9.2
Case B.			*Case I.*		
Oct. 2, 1909	4	4.6	Oct. 27, 1909	5	11.6
Oct. 6, 1909	3	6.3	Oct. 30, 1909	5	15.9
Mar. 2, 1910	11	6.6			
Average	..	5.8	Average	..	13.8
Case C.			*Case J.*		
Apr. 13, 1909	7	8.6	Oct. 4, 1909	3	7.0
May 14, 1909	7	7.9	Oct. 21, 1909	3	9.5
June 8, 1909	6	6.9	Oct. 22, 1909	5	9.2
June 11, 1909	6	16.0			
June 15, 1909	7	6.3	Average	..	8.6
June 18, 1909	7	11.5			
June 22, 1909	6	10.6	*Case K.*		
June 25, 1909	7	11.7	May 11, 1909	7	10.3
Oct. 25, 1909	3	15.3			
Oct. 26, 1909	5	9.5	*Case L.*		
Oct. 27, 1909	3	6.7	Jan. 1, 1909	8	8.8
Oct. 28, 1909	3	11.5	Jan. 9, 1909	8	9.4
Oct. 29, 1909	3	10.6	Jan. 26, 1909	8	9.0
Oct. 30, 1909	3	7.8	Feb. 11, 1909	9	9.6
Oct. 31, 1909	3	10.1	Mar. 27, 1909	6	10.7
Average	..	10.1	Average	..	9.5
Case D.			*Case M.*		
Oct. 1, 1909	3	11.3	Nov. 27, 1909	5	6.3
Oct. 5, 1909	3	11.9			
Oct. 14, 1909	3	8.8	Average:		
			Severe cases, A to J	..	9.6
Average	..	10.7	Light cases, K to M	..	8.7
			All cases	..	9.4
Case E.					
Nov. 9, 1908	8	10.4			
Nov. 16, 1908	8	11.7			
Average	..	11.1			

individual averages range from 4.3 milligrams with the woman subject, Mrs. B., to 9.6 milligrams with T. M. C., the average of all 10 subjects being 6.85 milligrams of nitrogen per kilogram of body-weight per hour. This value is nearly 30 per cent less than that found with the severe cases of diabetes.

TABLE 181.—*Nitrogen excretion of normal subjects per kilogram of body-weight per hour in periods without food.*

Subject.	Body-weight.	Number of experiments.	Minimum.	Maximum.	Average.
			mg.	*mg.*	*mg.*
Prof. C.	83.5	3	6.2	10.5	8.3
F. G. B.	83.0	2	6.9	7.4	7.1
H. F.	79.7	1	5.6	5.6	5.6
F. A. R.	74.4	5	4.1	6.3	5.0
J. J. C.	67.6	8	5.6	9.2	6.2
Mrs. B.	67.0	1	4.3	4.3	4.3
J. R.	66.0	12	3.8	8.7	6.5
L. E. E.	59.6	14	6.2	11.0	8.3
T. M. C.	49.0	3	7.9	10.8	9.6
Dr. R.	48.5	1	7.6	7.6	7.6
Average all subjects...	....	..	....	....	6.85

In a recent research, Johansson[1] has likewise determined the nitrogen excretion 12 hours or more after the last meal with a number of different subjects, all healthy young men. The results thus found are of interest in connection with the experiments here reported, and are given in table 182.

TABLE 182.—*Excretion of nitrogen per hour per kilogram of body-weight in periods without food (Johansson).*

	S-st (61 kilos.).	L-hl (58 kilos.).	E-d (57 kilos.).	L-M (85 kilos.).	W-d (73 kilos.).	Average of all experiments.
	mg.	*mg.*	*mg.*	*mg.*	*mg.*	*mg.*
Experiment A	9.6	10.9	7.5	6.5	7.8	8.5
Experiment B	8.7	9.1	....	6.4	9.7	

In these experiments, as in those cited in table 181, the variations on the same individual are very small, the subject W—d showing the widest fluctuation (a little less than 2 milligrams). The average for all the subjects is 8.5 milligrams per kilogram of body-weight per hour. This is but a little less than that found with the severe cases of diabetes.

Since, however, in making general comparisons between the results with normal individuals and with subjects having severe diabetes, we are using chiefly the individuals experimented upon in this laboratory, it is necessary to consider whether or not the increased nitrogen elimination clearly indicated by the diabetics when compared with our normal subjects could, in any way, affect the metabolism as a whole. In other words, was the increased protein katabolism

[1] Johansson. Skand. Archiv f. Physiologie, 1908, **21**, p. 1.

sufficient to result in the total katabolism being influenced by the specific dynamic action of the excess protein disintegrated? The difference between the average values found in the severe cases of diabetes and those found with 10 normal subjects in the Nutrition Laboratory was 9.60 — 6.85 = 2.75 milligrams. Assuming an average naked body-weight of 55 kilograms for the diabetics, we find that there would be an excess of 151 milligrams of nitrogen per hour. Since each gram of nitrogen in the form of protein gives rise to approximately 26 calories, this excess protein would result in the liberation of approximately 4 large calories of heat per hour. If we assume the most favorable conditions for the specific dynamic action of the protein to assert itself, and if we assume Rubner's value of 31 per cent as the extra heat dissipated and not available to the body, then there would be an excess of only about 1.5 calories eliminated as the result of the increased katabolism. This is barely 2 per cent of the total energy transformations, in any of these cases, and hence we are entirely unable to attribute the increased metabolism of 15 to 20 per cent to a possible increase in the protein katabolism, even by assuming the most favorable condition for the specific dynamic action of the protein to assert itself.

THE DEXTROSE-NITROGEN RATIO.

On the assumption that the nitrogen excreted in the urine of diabetics on a carbohydrate-free diet is derived from protein, the relationship between the nitrogen and dextrose excreted has been much used by different investigators in attempting to estimate the quantity of dextrose that may be formed from 100 grams of protein. For this purpose it is assumed that on a carbohydrate-free diet cases of severe diabetes give off from 1 to 4 grams of dextrose per gram of nitrogen in the urine. This ratio has been called the dextrose-nitrogen ratio. A very large number of experiments have been made upon this basis, but in most instances sufficient care was not taken to consider the possibility of the previous storage of sugar or glycogen in the body. With animals this has been possible, as the glycogen can be removed by methods which with men would be impossible. In all the experiments here reported, the dextrose-nitrogen ratio has been determined in the period in the early morning without food at least 12 hours after the last meal.

The errors incidental to determining this dextrose-nitrogen ratio are numerous. In the first place, the assumption that the nitrogen excreted in the urine is accompanied by the glucose or dextrose formed from the protein is difficult to prove since it presupposes a parallelism in the excretion of the two portions of the disintegrated protein molecule, namely, the nitrogenous and the non-nitrogenous portion. As can be seen in the experiments in which meat was fed, the excretion of the sugar is very much more rapid than of the nitrogen, the nitrogen excretion not increasing to the maximum for some hours, while the sugar excretion takes place almost immediately. This has been pointed out in numerous experiments on both man and animals by earlier writers.

It is probably true that the dextrose-nitrogen ratio determined 12 hours after the last meal is erroneous in that there is the influence of previously existing sugar or glycogen in the body, and the assumption that the sugar excreted under these conditions comes wholly from protein is not tenable. Fortunately, in connection with these experiments, we have a large number of these dextrose-nitrogen ratios determined in short periods in the early morning before food was taken. The variations in these dextrose-nitrogen ratios are most significant, and the results have been brought together in table 183 for comparison, together with the respiratory quotients.

TABLE 183.—*The dextrose-nitrogen ratio and respiratory quotient during periods without food.*

Case and number.	Date.	Time.	D:N.[1]	Respiratory quotient for experiment.[2]
	1908.			
Case A 1......	Nov. 4......	7h 00m a.m. to 8h 00m a.m....	4.71	0.70
		8 00 a.m. 10 00 a.m....	4.91	
		10 00 a.m. 12 00 noon...	4.71	
		12 00 noon 2 00 p.m....	4.20	
Case A 2......	Nov. 18......	7 00 a.m. 8 52 a.m....	4.88	.70
		8 52 a.m. 10 52 a.m....	4.30	
		10 52 a.m. 12 52 p.m....	2.91	
		12 52 p.m. 2 52 p.m....	1.92	
Case A 3......	Dec. 16......	7 00 a.m. 9 18 a.m....	3.39	.74
		9 18 a.m. 11 18 a.m....	2.83	
		11 18 a.m. 1 18 p.m....	2.40	
		1 18 p.m. 3 18 p.m....	1.11	
	1909.			
Case A 4......	Mar. 4......	7 00 a.m. 8 51 a.m....	8.57	.76
		8 51 a.m. 10 21 a.m....	7.57	
		10 21 a.m. 11 51 a.m....	6.29	
Case A 5a.....	Mar. 13......	7 00 a.m. 9 02 a.m....	8.26	.68
		9 02 a.m. 11 02 a.m....	7.53	
Case A 6......	Mar. 19......	7 00 a.m. 8 47 a.m....	8.33	.72
		8 47 a.m. 10 47 a.m....	7.41	
		10 47 a.m. 12 47 p.m....	5.73	
Case A 7......	Mar. 26......	7 00 a.m. 9 50 a.m....	8.21	.71
		9 50 a.m. 12 50 p.m....	5.51	
Case A 8......	May 17......	7 00 a.m. 9 26 a.m....	8.51	.66
		9 26 a.m. 11 26 a.m....	6.98	
		11 26 a.m. 1 30 p.m....	5.59	
	1910.			
Case A 16.....	Mar. 11......	7 00 a.m. 9 10 a.m....	9.74	.74
		9 10 a.m. 10 10 a.m....	9.74	
		10 10 a.m. 11 13 a.m....	9.43	
		11 13 a.m. 12 08 p.m....	8.63	

[1] The dextrose was determined for the periods by the Citron method. For a description of this method, see p. 26.

[2] These figures represent the average respiratory quotients for the measured periods on that day.

TABLE 183.—*The dextrose-nitrogen ratio and respiratory quotient during periods without food*—Continued.

Case and number.	Date.	Time.	D : N.	Respiratory quotient for experiment.
	1909.			
Case B 3......	Oct. 2......	$6^h 30^m$ a.m. to $10^h 00^m$ a.m....	0.00	0.75
Case B 4......	Oct. 6......	7 30 a.m. 10 00 a.m....	.91	.70
	1910.			
Case B 1......	Mar. 2......	7 30 a.m. 12 30 p.m....	2.69	.74
		12 30 p.m. 2 30 p.m....	.71	
		2 30 p.m. 6 45 p.m....	.29	
	1909.			
Case C 1......	Apr. 13......	6 00 a.m. 11 04 a.m....	3.47	.75
		11 04 a.m. 1 04 p.m....	1.74	
Case C 2......	May 14......	6 00 a.m. 10 44 a.m....	2.88	.75
		10 44 a.m. 1 05 p.m....	1.36	
Case C 3......	June 8......	5 45 a.m. 9 12 a.m....	12.37	.67
		9 12 a.m. 10 12 a.m....	9.36	
		10 12 a.m. 11 12 a.m....	8.61	
		11 12 a.m. 12 12 p.m....	6.82	
Case C 4......	June 11......	6 00 a.m. 8 16 a.m....	4.70	.69
		8 16 a.m. 10 16 a.m....	4.00	
		10 16 a.m. 11 16 a.m....	2.97	
		11 16 a.m. 12 16 p.m....	1.80	
Case C 5......	June 15......	6 00 a.m. 9 30 a.m....	11.29	.69
		9 30 a.m. 11 30 a.m....	9.56	
		11 30 a.m. 12 30 p.m....	7.45	
Case C 6......	June 18......	5 40 a.m. 7 20 a.m....	5.92	.74
		7 20 a.m. 10 32 a.m....	4.36	
		10 32 a.m. 12 32 p.m....	2.73	
Case C 7......	June 22......	5 00 a.m. 7 20 a.m....	8.97	.71
		7 20 a.m. 8 43 a.m....	7.19	
		8 43 a.m. 11 13 a.m....	5.99	
Case C 8......	June 25......	5 45 a.m. 10 00 a.m....	5.31	.71
		10 00 a.m. 10 53 a.m....	3.62	
		10 53 a.m. 1 00 p.m....	3.19	
Case C 19.....	Oct. 25......	7 00 a.m. 9 45 a.m....	5.50	.69
Case C 20.....	Oct. 26......	7 00 a.m. 9 31 a.m....	4.22	.71
Case C 9......		9 31 a.m. 10 28 a.m....	4.75	.73
		10 28 a.m. 11 28 a.m....	5.97	
		11 28 a.m. 12 28 p.m....	5.93	
Case C 21.....	Oct. 27......	7 15 a.m. 9 55 a.m....	10.10	.71
Case C 22.....	Oct. 28......	7 10 a.m. 9 25 a.m....	4.44	.66
		9 25 a.m. 10 09 a.m....	4.83	
Case C 23.....	Oct. 29......	7 00 a.m. 10 00 a.m....	4.21	.68
Case C 24.....	Oct. 30......	7 10 a.m. 10 15 a.m....	5.04	.70
Case C 25.....	Oct. 31......	7 00 a.m. 9 55 a.m....	2.61	.69
Case D 1......	Oct. 1......	7 00 a.m. 8 47 a.m....	3.21	.73
		8 47 a.m. 9 44 a.m....	2.86	
Case D 2......	Oct. 5......	9 55 a.m.	1.68	.74
Case D 3......	Oct. 14......	9 50 a.m.	4.96	.75

TABLE 183.—*The dextrose-nitrogen ratio and respiratory quotient during periods without food*—Continued.

Case and number.	Date.	Time.	D : N.	Respiratory quotient for experiment.
	1908.			
Case E 1......	Nov. 9......	$7^h 00^m$ a.m. to $9^h 02^m$ a.m....	6.15	0.72
		9 02 a.m. 11 02 a.m....	4.80	
		11 02 a.m. 1 02 p.m....	3.80	
		1 02 p.m. 3 02 p.m....	2.44	
Case E 2......	Nov. 16......	7 00 a.m. 9 21 a.m....	6.28	.74
		9 21 a.m. 11 21 a.m....	4.90	
		11 21 a.m. 1 21 p.m....	3.84	
		1 21 p.m. 3 21 p.m....	2.94	
Case F 1......	Nov. 11......	7 00 a.m. 8 50 a.m....	2.27	.74
		8 50 a.m. 10 50 a.m....	1.37	
		10 50 a.m. 12 50 p.m....	.73	
		12 50 p.m. 2 50 p.m....	.32	
	1909.			
Case G 1......	Feb. 16......	7 00 a.m. 9 46 a.m....	7.50	.73
		9 46 a.m. 11 52 a.m....	6.22	
		11 52 a.m. 2 55 p.m....	3.66	
	1910.			
Case H 1......	Feb. 1......	12 15 p.m.	9.94	.75
Case H 2......	Feb. 7......	12 15 p.m.	8.17	.79
Case H 3......	Feb. 9......	7 00 a.m. 10 00 a.m....	7.32	.81
		10 00 a.m. 2 20 p.m....	1.98	
Case H 4......	Feb. 12......	7 00 a.m. 9 15 a.m....	5.40	.72
		9 15 a.m. 1 00 p.m....	4.42	
Case H 5......	Mar. 5......	6 00 a.m. 12 45 p.m....	6.84	.76
	1909.			
Case I 1......	Oct. 27......	7 00 a.m. 9 14 a.m....	16.44	.76
		10 14 a.m. 11 18 a.m....	11.34	
Case J 3......	Oct. 4......	7 00 a.m. 10 15 a.m....	5.04	.85
Case J 1......	Oct. 22......	10 04 a.m.	5.00	.75
		10 04 a.m. 12 04 p.m....	3.24	
Case K 1......	May 11......	9 40 a.m.	.32	.76
		9 40 a.m. 11 40 a.m....	.36	
		11 40 a.m. 1 40 p.m....	.29	
Case L 1......	Jan. 1......	7 00 a.m. 9 52 a.m....	.63	.78
		9 52 a.m. 11 52 a.m....	.28	
		11 52 a.m. 1 52 p.m....	.22	
		1 52 p.m. 2 52 p.m....	.24	
Case L 2......	Jan. 9......	7 00 a.m. 8 50 a.m....	.47	.75
		8 50 a.m. 10 50 a.m....	.29	
		10 50 a.m. 12 50 p.m....	.25	
		12 50 p.m. 2 50 p.m....	.11	
Case L 3......	Jan. 26......	7 00 a.m. 8 55 a.m....	.25	.75
		8 55 a.m. 10 55 a.m....	.24	
		10 55 a.m. 12 56 p.m....	.27	
		12 56 p.m. 2 50 p.m....	.24	
Case L 4......	Feb. 11......	7 00 a.m. 1 25 p.m....	.12	.78
		1 25 p.m. 3 30 p.m....	.20	
Case L 5......	Mar. 27......	7 00 a.m. 9 07 a.m....	.16	.79
		9 07 a.m. 11 07 a.m....	.23	
		11 07 a.m. 1 07 p.m....	.17	

While there seems to be no definitely marked division in the relationship between the respiratory quotient and the dextrose-nitrogen ratio, there appears to be a general tendency for the dextrose-nitrogen ratio to be low when the respiratory quotient is high, and the ratio to be high when the respiratory quotient is low. One can perhaps readily understand why the first statement should be true, namely, that the dextrose-nitrogen ratio would be low when the respiratory quotient was high, because under those conditions the body is burning glycogen or burning carbohydrate as indicated by the high respiratory quotient. It can be assumed, therefore, that a larger amount of glycogen or sugar existing in the blood would be burned than under other conditions. To explain why there should be such a large excretion of sugar in the urine at times when the respiratory quotient is low is more difficult.

It can also be assumed that if the dextrose-nitrogen ratio is large the body would be flooded, so to speak, with sugar or glycogen, and the respiratory quotient would be larger. This is assuming that the flooding of the body by sugar, either from the liberation of the previously stored glycogen in the liver or from some other source, results in an increased oxidation, and also increased excretion of sugar in the urine. There may be a large part of this flooding from the liver pass into the urine, and also a sufficient part of it burned to increase the respiratory quotient. Obviously, these two views are contradictory, but they represent two possibilities that should be borne in mind in any final discussion.

From the foregoing discussion it would seem to be almost impossible to control experimental conditions on man so as to be certain of the value and scientific accuracy of any dextrose-nitrogen ratio. Considering the possibilities for the storage of glycogen in the liver of man, the impracticability of experimentally removing glycogen by any of the methods so often used for animals, and of subjecting diabetic patients, who are frequently critically ill, to a diet more strict and more one-sided than is commonly used in such cases, it can be seen that it is practically impossible to determine the dextrose-nitrogen ratio of man.

Lusk has suggested that if a meat-fat diet be adhered to for a number of days there may be under these conditions a dextrose-nitrogen ratio that is characteristic. A ratio with as high a value as 3.65 has been termed by him the "fatal" ratio. It is, however, not out of the bounds of possibility that even with a meat-fat diet persisted in for some time, the storage of glycogen may ultimately be drawn upon to such an extent as to seriously vitiate the accurate determination of any dextrose-nitrogen ratio, for with diabetics it is more than probable that any glycogen stored can be burned if there is an ultimate demand for it, as in very severe muscular work, or that it may be transformed to sugar and excreted as such. Even in the most severe cases of diabetes, glycogen has frequently been found in the liver, particularly after eating sugars, such as dextrose and levulose. We can consider, for example, that glycogen is held in the liver cells perhaps somewhat as creatine is held in the muscles. It was found that during fasting when muscle substance was broken down that creatine as

such was excreted in the urine, and a theory was propounded to explain this appearance of creatine in the urine on the ground that it accompanied the dissolution of muscular tissue, thus resulting in the liberation of creatine which was not converted to creatinine and excreted as such in the urine.

If we assume that glycogen is held in the liver or muscles in some similar way, it is not too great an assumption to make that under conditions of fasting there is body-material broken down and glycogen may be set free with the nitrogenous material of the tissue holding the glycogen. The glycogen may be in part burned and in part excreted as sugar. Obviously, therefore, in considering the dextrose-nitrogen ratio, we deal here with the possibility of a source of sugar not only in protein but likewise in glycogen liberated as the result of the disintegrated body-materials.

Thus, from another standpoint, it is seen that the dextrose-nitrogen ratio is very uncertain. Conditions such as are outlined above, however, would indicate somewhat higher rather than lower ratios. Consequently, all the factors of the dextrose-nitrogen ratio must be with man, at least, of little avail owing to the fact that we have no knowledge whatever with regard to the amount of glycogen present in the body at the time of the experiment. Studies of the dextrose-nitrogen ratios of man should invariably be accompanied by a careful series of especially planned respiration experiments, showing the amounts of materials actually burned on the experimental days. From the respiratory quotient it is possible to determine with considerable accuracy the kind of material burned, and if there are drafts upon body-glycogen or storage of body-glycogen this can readily be shown. It is impracticable to starve subjects with severe diabetes long enough to have the katabolism wholly of body-protein and body-fat, so we have no means of knowing what the dextrose-nitrogen ratio would be under these conditions. It is highly probable, however, that the body would utilize its material most economically in conformity with the experience found with fasting individuals, and that the dextrose-nitrogen ratio would never be very high. The subsequent effect of ingesting meat might be to increase this ratio somewhat. Experiments of this kind should be made and should be completely controlled by respiration experiments which would indicate the nature of the material burned.

Under these circumstances, therefore, we must hold in abeyance all judgment with regard to the dextrose-nitrogen ratio thus far determined on man. As a matter of fact, it can readily be seen that these ratios throw no light whatever upon the possibility of the formation of carbohydrate from protein or sugar from fat, or, indeed, from the relative amounts of sugar formed from 100 grams of albumen.

It seems to be very clear from the marked falling off in the dextrose-nitrogen ratio in most of the experiments that the sugar excretion in the first period is certainly influenced by a previous condition of glycogen or sugar surplus in the body. With animals by the use of cold, strychnine, phloridzin, or removal

of the pancreas it is possible to remove a very large proportion of glycogen from the body; with man it is impossible to use these methods, and we must never forget that there may be considerable quantities of glycogen which can be drawn upon immediately when required by the demands of the subject's body. In many instances, this glycogen may be used and rapidly replaced; in others, it may be very slowly replaced. Indeed, it may be dangerous to starve a patient with severe diabetes or even to place him upon a strict meat-fat diet for several days to determine the dextrose-nitrogen ratio.

RESPIRATORY QUOTIENT IN DIABETES.

The relationship between the volumes of carbon dioxide excreted and of oxygen consumed is of great significance in interpreting metabolism during diabetes, and this relationship has been most carefully discussed by Magnus-Levy[1] who determined with great care the respiratory quotient in a number of cases of diabetes.

As pointed out in earlier sections of this report, the determination of the carbon-dioxide elimination in practically every experiment is carried out with the greatest degree of exactness, and can, for the most part, be relied upon absolutely. On the other hand, the determination of the oxygen consumption involving as it does more or less absence of muscular activity and requiring accurate measurements of temperature inside the chamber, are at times inaccurate. Obviously, an erroneous oxygen determination will result in an erroneous respiratory quotient. While individual experiments may be unreliable, fortunately in the experiments here reported, there is a sufficiently large number of observations from which to draw positive deductions with regard to the average respiratory quotients of different individuals. The respiratory quotients in all of our experiments with diabetics without food have been collected in table 184.

While an examination of the results shows notable variations in the respiratory quotient with individual experiments ranging in Case A from 0.66 to 0.76, the average of all results with each subject is relatively constant. In general, the most severe cases have somewhat lower respiratory quotients than the light cases. The striking exception to this is Case H, who had an average respiratory quotient of 0.77. On the other hand, Case K had an unusually low respiratory quotient with the respiration apparatus. Since but one experiment was made with this subject, however, too much value can not be placed upon so small an amount of data. Obviously, it is necessary to consider the average of the light cases with the respiration apparatus as practically without significance, as it is based wholly upon the one experiment with Case K.

The lowest respiratory quotient found was 0.64 in one experiment with Case C and the highest, 0.81, with Case H. Although a number of respiratory quotients below 0.7 are given, there is nothing in the experiments to prove that this

[1] Magnus-Levy, Zeit. f. klin. Med., **56**, 1905, p. 83.

is an absolutely accurate indication of the respiratory exchange with these individuals at this time. We have no reason to believe, therefore, that the average values found with these subjects do not represent more truly than the individual values the actual conditions at any particular time. Unusually low respiratory quotients of 0.6 or below we have not found, and we have no ground for believing that in any of the cases here examined was the metabolism so disturbed as to affect the relation between the carbon dioxide excreted and the oxygen consumed to such an extent as to produce a respiratory quotient below 0.6.

TABLE 184.—*Average respiratory quotients in experiments with diabetics without food.*

	Calorimeter.		Respiration apparatus.	
Subject.	Respiratory quotient.	Average.	Respiratory quotient.	Average.
Severe diabetes.				
Case A	0.75 0.75 0.74 0.76 0.68 0.72 0.71 0.66 0.73 0.74	0.71	....	....
B	0.74	0.74	0.71 0.75 0.70	0.72
C	0.75 0.75 0.67 0.69 0.69 0.74 0.71 0.71 0.72	0.71	0.70 0.64 0.71 0.68 0.67 0.71 0.69 0.71 0.71 0.66 0.68 0.70 0.69	0.69
D	....	....	0.73 0.74 0.75	0.74
E	0.72 0.74	0.73	....	...
F	0.74	0.74	....	...
G	0.73	0.73	....	...
H	0.75 0.79 0.81 0.72 0.76	0.77	0.76	0.76
I	0.76 0.72	0.74	....	...
J	0.75	0.75	....	...
Av. of severe cases	....	0.74	....	0.73
Light diabetes.				
Case K	0.76	0.76	0.70	0.70
L	0.78 0.75 0.75 0.78 0.79	0.77	....	....
M	0.78 0.78 0.72	0.76	....	....
Av. of light cases	....	0.76	....	0.70
Av. of all cases	....	**0.74**	....	**0.72**

The respiratory quotient, therefore, in severe cases of diabetes, indicates practically a fat katabolism compensated on one hand by a slight increase due to the protein katabolism, and on the other hand by the increase in the formation of sugar from protein, since with pure fat the respiratory quotient would be 0.711, while with pure carbohydrate it is 1.00. Assuming that the protein metabolism is 15 to 20 per cent of the total, we find that the respiratory quotient would be not far from 0.73, which is the average of practically all the severe cases. As has been pointed out by Magnus-Levy,[1] however, other factors play an important

[1] For an interesting theoretical discussion of these points, see Magnus-Levy, *loc. cit.*, p. 93.

rôle here, such as the formation of partially oxidized material as acetone bodies and the excretion of sugar in the urine.

It should be stated that although alcohol was used sparingly in many of the diets, it was not used for 12 hours prior to these experiments without food, and hence there can be no effect of the naturally low respiratory quotient following the taking of alcohol.

In studying the respiratory quotient of diabetics, it is hardly probable that when we find somewhat higher respiratory quotients, it indicates that the diet of the preceding day had a marked influence upon the respiratory quotient 12 hours after the last meal, a condition frequently noted in this laboratory in experiments. In a series of unpublished experiments carried out by Benedict, Riche and Emmes, it has been found that the respiratory quotient is noticeably higher on days following a carbohydrate diet than on days following a fat diet, although the respiratory quotient in no case was determined less than 12 hours after the last meal. With diabetics, with a relatively low carbohydrate ingestion, and with a relatively low capability for storing carbohydrate, it is probable that no such influence exists for any great length of time. It is significant, however, that in many instances the dextrose-nitrogen ratio is of such a character as to indicate a sweeping of carbohydrate out of the system. While the evidence points to a greatly retarded combustion of carbohydrates by diabetics and the possibility that previously ingested carbohydrate is but slowly oxidized, yet, on the other hand, that the increase in sugar excretion in the urine is not due to previously stored glycogen has not been proved. Experiments in which a large carbohydrate diet is given on a day or two prior to the "nüchtern" experiments should therefore be made and the respiratory quotient studied, together with the dextrose-nitrogen ratio, to determine this point.

THE RESPIRATORY QUOTIENT AS AN INDEX OF THE CHARACTER OF THE KATABOLISM.

Since a respiratory quotient appreciably above 0.7 indicates an oxidation in part of carbohydrate, it may naturally be queried why, as the experiment continues, the respiratory quotient does not progressively sink, as the supply of glycogen or carbohydrate is being steadily drawn upon. As a matter of fact, in the experiments with normal subjects where relatively large storages of glycogen are present, the respiratory quotient remains relatively constant for 8 to 10 successive 1-hour periods.

In these experiments it has been repeatedly pointed out that individual respiration experiments are not to be taken as a criterion of the exact conditions at that time, as the experimental conditions were not ideal for obtaining accurate results for such short periods. Only the average of a large number of experiments can be really relied upon.

How much influence a relatively small amount of carbohydrate exerts upon the respiratory quotient may be seen if we calculate the metabolism of an indi-

vidual, eliminating approximately 25 grams of carbon dioxide per hour, or not far from 80 to 90 calories. If we assume the katabolism of protein to be 3.5 grams, and of fat, 7 grams, and compute the respiratory quotient from the combustion of the material, using the data given in table 160 on page 166, and then compute the respiratory quotient under similar conditions, where the amount of protein burned is the same, but 0.9 of a gram of fat is replaced by the isodynamic quantity, namely, 2 grams of carbohydrate, we can see a noticeable difference in the respiratory quotient.

TABLE 185.—*Influence of carbohydrates on the respiratory quotient.*

Material katabolized.	Carbon dioxide produced.	Oxygen consumed.
PROTEIN-FAT KATABOLISM.		
	grams.	*grams.*
Protein (3.5 grams)	5.32	4.78
Fat (7 grams)	19.53	19.91
Total	24.85	24.69
Total liters	12.65	17.28
Respiratory quotient	0.73	....
PROTEIN-FAT-CARBOHYDRATE KATABOLISM.		
Protein (3.5 grams)	5.32	4.78
Fat (6.1 grams)	17.02	17.35
Carbohydrate (2 grams)	3.26	2.37
Total	25.60	24.50
Total liters	13.03	17.15
Respiratory quotient	0.76	.....

In other words, the combustion of 2 grams of carbohydrate per hour results in an increase in the respiratory quotient from 0.73 obtained when no carbohydrate was burned, to 0.76 in the carbohydrate period. Two grams of carbohydrate per hour corresponds to a combustion of about 50 grams per day. It is not to be inferred, from this computation, however, that all diabetics who burn 2 grams of carbohydrate per hour should give a respiratory quotient of 0.76, for, as has been assumed by Magnus-Levy and others, the formation of B-oxybutyric acid and other unoxidizable materials in the body has a distinct tendency to lower the respiratory quotient and instead of having a protein-fat respiratory quotient of 0.73, we would probably have somewhat lower values. In these calculations, which are given in detail in table 185, it is assumed that the protein katabolism is about 15 to 20 per cent of the total katabolism.

VAPORIZATION OF WATER FROM THE LUNGS AND SKIN IN DIABETES.

From the large amount of water passing through the body of a diabetic, one might naturally infer that there was a disturbance in the normal amount of water vaporized from the lungs and skin. To oppose this assumption there is the fact that the skin of diabetics is usually very dry. The observations made in connection with the metabolism experiments here reported enable us to directly determine the water vaporized from the lungs and skin, and the results have been brought together and computed on the basis of per square meter of body-surface per hour. Furthermore, since a certain amount of heat is required to vaporize the water, the proportion of the total heat eliminated required to vaporize this water has also been computed. For comparison, the average of nine experiments with normal individuals is given. The results are given in table 186.

TABLE 186.—*Water vaporized and proportion of total heat required for the vaporization in experiments with diabetics.*

[Average amounts.]

Subject.	Body-weight without clothing.	Body surface.[1]	Water vaporized per square meter per hour.	Proportion of heat eliminated used to vaporize water.
	kilos.	*sq. meters*	*grams.*	*p. ct.*
Severe diabetes.				
Case A	52.6	1.73	14.1	20.2
C	62.3	1.93	15.8	22.2
I	45.2	1.56	18.5	22.7
J	53.7	1.75	21.8	30.7
Average of severe cases	....	....	17.6	24.0
Light diabetes.				
Case K	60.6	1.90	20.0	27.9
L	64.3	1.98	13.9	18.6
M	82.3	2.33	11.6	19.9
Average of light cases	....	....	15.2	22.1
Average of all cases	....	....	16.5	23.2
Average of 9 normal individuals	....	....	15.3	22.5

[1] In computing body-surface, the formula of Meeh has been used: $12.312\sqrt[3]{\text{body-weight}}$.

It is seen that with the severe cases, the water vaporized per square meter of body-surface per hour was on the average, 17.6 grams, and 24 per cent of the total heat eliminated was used in vaporizing this water. With the light cases of diabetes it was somewhat less in amount, the difference, however, being almost wholly explained by the abnormally low values found with Case M, who was stout. The average of all cases for water vaporized per hour was 16.5 grams, and 23.2 per cent of the total heat eliminated was required to vaporize this water. The average of the results obtained with nine normal individuals showed that 15.3 grams of water per square meter of body-surface were vaporized per hour,

and of the total heat 22.5 per cent was required to vaporize this water. It is thus seen that the differences between diabetics and normal individuals wholly disappear as the slight mathematical differences, we believe, are without physiological significance.

While such short experiments are hardly comparable to the long experiments of Pettenkofer and Voit, it is of interest to note that the results found in all experiments do not confirm the belief obtained by these earlier writers from their experiments that the water vaporized by a diabetic is usually less than normal.

INFLUENCE OF THE INGESTION OF FOOD ON METABOLISM IN DIABETES.

With normal individuals there are two indices of metabolism affected by the ingestion of food, namely, the excretion of nitrogen in the urine and the respiratory quotient. When nitrogenous substances are ingested, there is usually an increase in the nitrogen excretion in the urine in a relatively short time after the ingestion of the food. When carbohydrate material is ingested, particularly in a state of fast, there is usually a noticeable increase in the respiratory quotient, that is, an increase in the carbon-dioxide production unaccompanied by a corresponding increase in the oxygen absorption. Knowing the influence of the ingestion of food on metabolism with normal individuals, it is extremely interesting to study its influence on metabolism in diabetes. Furthermore, diabetes adds one other interesting factor, inasmuch as there is excreted in the urine a portion of the material ingested, *i. e.,* sugar either preformed or resulting from protein katabolism. With severe diabetes, in which there is no tolerance for carbohydrate, the excretion of sugar in the urine after its ingestion is almost immediate.

INFLUENCE ON THE NITROGEN AND SUGAR EXCRETIONS.

In the cases here studied, many experiments were made in which no food was given; in others, relatively large amounts of cooked beefsteak, or of carbohydrate, usually of dextrose, and bread were ingested. The influence on the nitrogen and sugar excretions per hour from the ingestion of these materials is clearly shown by the results given in table 187, in which are reported, first, the average values found when no food was taken, both for the excretion of nitrogen per hour and the sugar per hour, then the excretion in the individual experiments when food was given.

With Case A it is seen that under ordinary conditions when food was not taken, there was 0.38 gram of nitrogen excreted per hour in the urine accompanied by 2.5 grams of sugar. The ingestion of about 225 grams of meat more than doubled the nitrogen excretion, and the sugar excretion was increased to 4.4 grams per hour. The observations usually covered from 3 to 6 hours. When carbohydrates were given, as in the form of dextrose and bread, the nitrogen excretion was but slightly affected, being, on the average, 0.50 gram, but the sugar excretion was noticeably influenced, the average increasing from 2.5 to

7.7 grams. The experimental periods in the carbohydrate experiments were likewise approximately 6 hours.

Assuming in this case that 225 grams of meat, corresponding to 56 grams of protein, could possibly yield 45 grams of sugar, provided that the maximum theoretical conversion of protein to sugar can here be taken, it is seen that in 6 hours about 12 grams out of the 45 grams of sugar were excreted. With the dextrose it was computed that about 70 grams of carbohydrates were ingested. Under these circumstances, therefore, there was an increase in the sugar excretion amounting to about 5 grams per hour, or 30 grams in 6 hours. It would

TABLE 187.—*Influence of the ingestion of food on the excretion of nitrogen and sugar in the urine of diabetics.*

[Amounts per hour.]

Subject.	Diet.	Experiments.	Nitrogen.	Sugar.
			grams.	*grams.*
Case A...	Without food..........	9 experiments	0.38	2.5
	Beefsteak [1]	A 10	.88	4.4
		A 11	.81	3.5
		A 14	.85	5.5
		A 15	.74	4.0
	Average A 10, 11, 14, 15	....	.82	4.4
	Carbohydrate [2]	A 5b	.56	9.0
		A 12	.46	7.0
		A 13	.47	7.0
	Average A 5b, 12, 13...	....	.50	7.7
Case C...	Without food..........	10 experiments	.55	2.7
	Beefsteak [3]	C 10	1.04	3.1
	Oatmeal [4]	C 11	.60	7.6
Case E...	Without food..........	2 experiments	.67	3.2
	Beefsteak [5]	E 3	.89	4.1
		E 4	1.16	5.7
	Average E 3, 4........	....	1.03	4.9
Case F...	Without food..........	F 1	.59	.7
	Beefsteak [6]	F 2	1.63	4.3
Case G...	Without food..........	G 1	.57	3.1
	Beefsteak [7]	G 3	1.25	8.6
	Carbohydrate [2]	G 2	.61	11.9

[1] Amounts of beeksteak eaten varied from 220 to 261 grams.
[2] Subject ate 75 grams of white bread and 25 grams of dextrose in each experiment (70 grams carbohydrates).
[3] Subject ate 253 grams of beefsteak.
[4] Subject ate 545 grams of cooked oatmeal containing 50-60 grams of carbohydrates.
[5] Amounts of beefsteak eaten were 329 and 402 grams.
[6] Subject ate 466 grams of beefsteak.
[7] Subject ate 546 grams of beefsteak.

appear, then, that with this particular subject, the sugar formed from protein was oxidized more readily than carbohydrates given as such, and that in the former case 33 grams out of a possible 45 were not excreted in 6 hours after the ingestion of food, while in the second case 30 grams out of 70 were not excreted. Furthermore, as the disintegration of protein is much slower, usually, than the absorption of carbohydrates, it is possible that the total sugar excretion from the protein katabolism had not taken place at the end of the 6-hour period, although the dextrose-nitrogen ratio would indicate a much more rapid excretion of the sugar than of the nitrogen-containing portion of the protein molecule.

In the above calculation, a maximum theoretical production of sugar from the protein has been assumed, and that from 56 grams of protein there would be formed 45 grams of sugar. Using the lower value of Minkowski, who assumes that only about 45 per cent of the protein can be converted into sugar, we would expect to find from the 56 grams of protein about 25 grams of sugar. On this basis, therefore, we can see that 12 grams out of the 25 were excreted in 6 hours, or only about half of the material ingested was burned. Under these circumstances, therefore, it would appear that the carbohydrate combustion by this diabetic was much the same whether sugar was given or whether the sugar was formed from protein, with perhaps a slight advantage in favor of the protein.

With Case C, the average nitrogen and sugar excretions when no food was being taken were 0.55 gram of nitrogen and 2.7 grams of sugar. When 253 grams of beefsteak were eaten, the excretion of nitrogen was doubled, reaching 1.04 grams, while the sugar excretion only rose to 3.1 grams, an almost insignificant rise. It is to be noted, however, that this period was only 4½ hours long, and that possibly a longer period might have resulted in a larger excretion of sugar in the urine. With this subject, instead of using bread and dextrose, 545 grams of cooked oatmeal, corresponding to 50 to 60 grams of carbohydrate, were ingested prior to one of the experiments. Under these circumstances, the hourly nitrogen excretion increased slightly, *i. e.*, from 0.55 gram to 0.60 gram, but there was a noticeable rise in the sugar excretion from 2.7 grams to 7.6 grams. This food experiment continued for only 2 hours, from $11^h\ 04^m$ a. m. to $1^h\ 04^m$ p. m., and it is highly probable that the sugar excretion did not reach the maximum in this time. Nevertheless, of the 50 to 60 grams of carbohydrate ingested at 11 a. m. but about 10 grams had appeared in the urine 2 hours later. With such a general intolerance for carbohydrates exhibited by this subject, as shown by the carbohydrate balances on the statistical chart, one would expect to find a large excretion of sugar almost immediately after the ingestion of carbohydrates, and we probably deal here with conditions which are frequently mentioned by earlier writers, when the ingested carbohydrate was not recovered in the urine and the inference was drawn that the carbohydrate was actually burned.

Unfortunately, experiments with bread and dextrose were not made with this man, and hence we have not the data for comparing the effects of these kinds of carbohydrates.

With Case E, experiments were made without food, and also after the ingestion of beefsteak. The nitrogen excretion was noticeably increased by the ingestion of the beefsteak, rising from 0.67 grams on the average to 1.03 grams. The sugar excretion, on the other hand, only underwent a moderate increase from 3.2 grams to 4.9 grams, showing that this subject was able to oxidize sugar from the non-nitrogenous portion of the protein with relative ease.

With Case F, the ingestion of beefsteak increased the nitrogen excretion nearly threefold, and the relatively low hourly sugar excretion of 0.7 gram per hour rose to 4.3 grams. From the amount of steak taken and the possible carbohydrate which was formed from the protein, it is seen that this subject oxidized, relatively speaking, the greater part of the non-nitrogenous portion of the protein molecule.

With Case G, the nitrogen output per hour was more than doubled by the ingestion of beefsteak, while the sugar output increased from 3.1 grams to 8.6 grams. Judging from the amount of beefsteak eaten, 546 grams, the excretion of the sugar in the urine over and above the amount noticed when food was not taken, was not sufficient to indicate the excretion of a large part of the non-nitrogenous portion of the steak in the urine. When carbohydrate in the form of dextrose and bread was ingested, the nitrogen excretion was hardly affected, while there was an enormous increase in the sugar in the urine per hour, which rose from 3.1 grams when without food to 11.9 grams, showing that the ability to either oxidize or store this form of carbohydrate material was almost wholly absent.

INFLUENCE ON THE RESPIRATORY EXCHANGE AND ON THE TOTAL KATABOLISM.

In addition to studying the influence of food upon the nitrogen and sugar excretions in the urine, we have also the means for determining the influence upon the carbon-dioxide excretion, oxygen consumption, and heat-production. It has been found with normal individuals that when food is ingested there is usually an increased katabolism as a whole. It has likewise been found that the different nutrients exercise a widely varying influence. Thus, while carbohydrate and fat produce a relatively slight increase in the total katabolism, when protein is ingested, there is a noticeable increase. With normal individuals, when carbohydrate is ingested several hours after the last meal is taken, there is almost immediately an increase in the carbon-dioxide excretion and a corresponding increase in the respiratory quotient. When protein is ingested, there is invariably an increase in the total katabolism, but there may or may not be a change in the respiratory quotient.

The plan of these experiments on the ingestion of food was not ideal for studying this particular subject, and as the problem was incidental to a more fundamental study of the general metabolism, it was deemed unwise to alter the

plans in order to enter into a scheme for studying such problems as the influence of the ingestion of food on the metabolism of diabetics. In these experiments, therefore, fasting values were determined in a number of experiments separately, and then on other experimental days either carbohydrate or protein food was ingested.

On this basis, it is necessary to assume that the metabolism prior to the ingestion of food was that of the preceding days when the fasting value was obtained. While with normal individuals this procedure is open to serious criticism, with diabetics whose metabolism is essentially the same from day to day, particularly when the diet contained minimum amounts of carbohydrates each day, this assumption is probably not far from correct. Since the results of experiments considered individually can not have much value, and the average results of a number of experiments should be used invariably in studies of this kind, the average values for carbon dioxide- and heat-elimination and for oxygen consumption found with different conditions of diet have been collected in table 188. In this table, also, are recorded the difference between the values found when no food was given and when carbohydrates or beefsteak were ingested, together with the percentage variations, using the value without food as the basis of comparison.

TABLE 188.—*Influence of the ingestion of food on the metabolism of diabetics.*

[Average amounts per kilogram of body-weight.]

Subject.	Diet.	No. of expts.	Carbon dioxide eliminated.			Oxygen absorbed.			Heat eliminated.		
			Per minute.	Compared with fasting.		Per minute.	Compared with fasting.		Per hour.	Compared with fasting.	
			c. c.	*c. c.*	*p. ct.*	*c. c.*	*c. c.*	*p. ct.*	*cals.*	*cals.*	*p. ct.*
Case A...	Without food...	9	3.28	....	....	4.62	....	....	1.34	....	....
	Carbohydrate [1].	3	3.23	−0.05	− 1.5	4.39	− .23	− 5.0	1.33	−0.01	− .7
	Beefsteak [2]	4	3.78	+0.50	+15.2	5.23	+ .58	+12.5	1.50	+0.14	+10.3
Case C...	Without food [3].	1	3.22	....	....	4.31	....	....	1.23	....	....
	Beefsteak [4]	1	3.46	+0.24	+ 7.5	4.85	+ .54	+12.5	1.30	+0.07	+ 5.7
	Without food [5].	1	3.24	....	....	4.54	....	....	1.26	....	....
	Oatmeal [6]	1	3.12	−0.12	− 3.7	4.47	− .07	− 1.5	1.30	+0.04	+ 3.2
Case E...	Without food...	2	3.29	....	....	4.53	....	....	1.34	....	....
	Beefsteak [7]	2	3.84	+0.55	+16.7	5.49	+ .96	+21.2	1.50	+0.16	+11.9
Case F...	Without food...	1	3.44	....	....	4.66	....	....	1.39	....	....
	Beefsteak [8]	1	4.24	+0.80	+23.3	5.76	+1.10	+23.6	1.64	+0.25	+18.0
Case G...	Carbohydrate [1].	1	3.13	....	....	3.92	....	....	1.33	....	....
	Beefsteak [9]	1	3.82	+0.69	[10] +22.0	5.19	+1.27	[10] +32.4	1.51	+0.18	[10] +13.5

[1] Subject ate 75 grams of white bread and 25 grams of dextrose in each experiment = 70 grams of carbohydrates.
[2] Amounts of beefsteak eaten varied from 220 to 261 grams.
[3] Experiment of May 14, 1909.
[4] Subject ate 253 grams of beefsteak.
[5] Experiment of May 27, 1909.
[6] Subject ate 545 grams of cooked oatmeal containing 50-60 grams of carbohydrates.
[7] Amounts of beefsteak eaten were 329 and 402 grams.
[8] Subject ate 466 grams of beefsteak.
[9] Subject ate 546 grams of beefsteak.
[10] Carbohydrate metabolism used as a basis.

With Case A, nine experiments were made in which the subject was without food, three experiments in which carbohydrates were given, and four experi-

ments in which beefsteak was ingested. In these experiments it is seen that the ingestion of approximately 70 grams of carbohydrate made no appreciable change in the metabolism as a whole. As a matter of fact, it so happens that there was a slight decrease in all of the factors measured after the ingestion of carbohydrate, a decrease, however, that is so slight that it is not probably of physiological importance. On the other hand, when beefsteak was ingested, there was a material increase in the carbon-dioxide excretion, oxygen consumption, and heat-elimination of 15.2, 12.5, and 10.3 per cent, respectively. As pointed out above, these experiments were not primarily designed to study this problem, for otherwise the experimental periods should have been longer, but it is well known that the stimulating increase in metabolism as the result of the ingestion of protein may continue over periods much longer than 6 hours, and thus the effect here noted may be somewhat below the maximum. These experiments were not longer than 6 hours, owing to the inability of the patients to withstand a longer sojourn in the chamber without weariness. Subsequently, indeed, the experiments were shortened to 3 hours. However, the results point toward a positive increase in metabolism as a whole upon the ingestion of protein, and no variation in metabolism from the ingestion of 70 grams of carbohydrate.

With Case C, but two experiments are available, one in which 253 grams of beefsteak were taken, and a second in which 545 grams of cooked oatmeal were ingested. Notwithstanding the ingestion of the 50 to 60 grams of carbohydrate in the form of oatmeal, it is seen that there was practically no increase in the metabolism, and the results are in full accord with those found with Case A. On the other hand, when beefsteak was given, there was an increase in metabolism amounting to 7.5 per cent in the carbon dioxide, 12.5 per cent of oxygen, and 5.7 per cent of heat, an increase proportionately much less than that found with Case A, who consumed the same amount of meat. The experience with this subject is suggestive of the possibility of the specific dynamic action of protein being somewhat affected by the abnormal metabolism in certain severe cases of diabetes. The detailed statistics for the first beefsteak experiment with Case A also implies a diminished influence of protein. Further study of this question is much desired.

With Case E, two experiments were made in which beefsteak was eaten, and we have also two experiments without food for comparison. Both of these were made in the month of November, 1908. In these two experiments he consumed 329 and 402 grams of beefsteak, respectively, and as the result of the ingestion of this beefsteak, the katabolism, as measured by the carbon-dioxide output, was increased by 16.7 per cent, the oxygen by 21.2 per cent, and the heat-elimination by 11.9 per cent, these values more nearly approximating those found with Case A.

A beefsteak experiment was also made with Case F, in which he ate 466 grams of steak, a much larger amount than was consumed by any of the previous subjects. The increase in metabolism was very noticeable, being 23.3 per cent in the carbon dioxide, 23.6 per cent in the oxygen, and 18 per cent in the heat, values somewhat larger than those found on the average with either of the preceding subjects, but which were comparable in a way with the increased quantity of steak eaten.

With Case G the comparisons are, unfortunately, not very satisfactory. The fasting experiment was made in the bed calorimeter, and owing to his discomfort and apprehension the metabolism as a whole was very much larger than would ordinarily be expected with this subject. Indeed, in a subsequent experiment made in the chair calorimeter, when carbohydrates were ingested, the metabolism was somewhat lower than in the bed calorimeter. While, therefore, the values found here without food with the bed calorimeter are probably very much higher than would naturally be expected with this apparatus, they are doubtless not far from the values which would be found for this subject in the chair calorimeter, for as has been seen from the experiments on other subjects, the ingestion of carbohydrate has practically no influence. Consequently, we can use with this subject the values found in the carbohydrate experiments as the base line in considering the values found in the chair calorimeter. On this basis, it can be seen that as the result of the ingestion of 546 grams of beefsteak, there was a noticeable increase in metabolism amounting to 22 per cent of the carbon dioxide, 32.4 per cent of the oxygen, and 13.5 per cent of the heat eliminated. The irregularities in these increments may in part be accounted for by the fact that but two experiments are here being compared and irregularities in individual experiments are frequently met with.

In some unpublished experiments on the influence of the ingestion of food on metabolism, made in the laboratory of Wesleyan University by Benedict and Carpenter, the amounts of food eaten, both carbohydrate and protein, were much larger than the amounts eaten in these experiments. But in one experiment, where 217 grams of beefsteak were eaten, it is interesting to note that the increase in katabolism was found to be 11 per cent in the carbon dioxide, 20 per cent in the oxygen, and some 8 per cent in the heat-elimination. The apparent discrepancy in these values has been the subject of much discussion, and the point to be emphasized here is that these results are not far from those found by actual experiments with diabetics. These results, however, were obtained in only one experiment made with one subject. The other experiments, in which more than 217 grams of meat were eaten, show much more uniform results for the three factors of metabolism.

GENERAL CONCLUSIONS REGARDING THE INFLUENCE OF THE INGESTION OF FOOD IN DIABETES.

The more or less fragmentary evidence secured in connection with these experiments points towards certain deductions.

In the severe cases of diabetes with which these experiments were made, the ingestion of carbohydrate produced no very material alteration in the metabolism as a whole. It is unfortunate that the experiments were so conducted that the respiratory quotients could not be determined with the respiration apparatus in short periods after the ingestion of a definite amount of food, but this was not feasible at the time the experiments were made.

The ingestion of large quantities of protein resulted in a marked increase in the total katabolism as measured by the three factors, carbon-dioxide excretion, oxygen consumption, and heat-elimination.

From a close inspection of the short periods in different experiments where carbohydrates were ingested, no evidence can be found of a combustion of carbohydrate as indicated by an increased carbon-dioxide excretion following ingestion. If such were found, it would be a reasonably accurate demonstration of the combustion of carbohydrate supplanting a portion of the katabolism normally progressing with the diabetes.

Experiments are much needed in which the gaseous exchange can be studied in short periods after the ingestion of food, particularly after the ingestion of protein, and also the possible effect of the ingestion of different proteins and various forms of carbohydrate, particularly oatmeal. It is conceivable, for example, that the protein of egg or of gluten or of meat may not have altogether the same action, particularly in grave cases of diabetes. The newly stimulated interest in the composition of the proteids and their food values is certain to result ultimately in experiments on pathological cases presenting such abnormal phases of metabolism as are found in grave cases of diabetes.

The ingestion of carbohydrate has no appreciable influence on the nitrogen excretion of a diabetic. The ingestion of protein results in a noticeable increase as would be expected from the nitrogenous nature of the protein molecule.

The excretion of sugar during the early morning hours without food is somewhat increased by the ingestion of meat, while the ingestion of carbohydrates as such usually produces a marked increase in the sugar in the urine. Indeed, in certain instances it would appear as if the non-nitrogenous portion of the protein molecule, *i. e.,* the portion that is ordinarily considered as being converted into sugar and excreted as such, is much more readily burned by diabetics than is ingested preformed sugar.

With normal individuals the ingestion of protein produced certain effects which were not apparent with diabetics, namely, accelerated pulse- and respiration-rates, and a greater uneasiness of body-position. In practically all of the experiments with diabetics after the ingestion of beefsteak, except in those with

Case G, there was apparent no material influence upon the pulse- or respiration-rates. In spite of this fact, there was still a noticeable increase in the total katabolism as a whole. The reason for the absence of increased pulse- or respiration-rates in connection with this increased metabolism is at best somewhat obscure. Further experiments will be made in which more careful and continuous records of the pulse- and respiration-rates, and, indeed, blood-pressure will be secured, as well as a most careful series of observations with regard to the body-muscular movements. It would seem hardly probable that there could be an increase of metabolism without increased pulse- or respiration-rates, and yet these experiments seem to imply that this was the case with these diabetics. With normal individuals, the ingestion of even moderate amounts of protein invariably results in a noticeable increase in both the pulse- and respiration-rates.

POSSIBLE INFLUENCE OF THE INGESTION OF COFFEE.

A criticism may possibly be made of these studies on account of the fact that in almost every case the subjects took clear, black coffee prior to the experiment, usually from 1 to 2 hours before the actual experimental period began. In a number of experiments made in Middletown by Benedict and Carpenter, as yet unpublished, the ingestion of coffee infusion resulted in no appreciable influence on metabolism. In one experiment where large amounts of hot coffee were consumed during the progress of the experiment, and the muscular exercise involved in going to and from the food aperture played an important rôle, there was an increase in metabolism, but in all other experiments this increase did not appear. We believe that it is hardly probable that coffee taken an hour or more before the beginning of the actual experimental period could have played any material rôle in the metabolism, or that any increase in metabolism found in diabetics over the normal can not be explained as resulting even to a very small degree from the influence of the coffee ingested an hour or more before the experiment began.

One possible influence of the ingestion of coffee in this research, however, should not be overlooked, that is the effect of the presence of sugar-forming material in the coffee infusion upon the determination of the dextrose-nitrogen ratios in certain of the experiments. For a series of experiments made in Middletown, Connecticut, a large number of analyses of coffee were made. It was found as the result of these experiments that coffee as ordinarily made contains about 10 grams of solid matter per liter of infusion.

An analysis of the infusion ordinarily used at the New England Deaconess Hospital showed in two samples an average of 1.13 per cent of dry matter. Hydrolyzing portions of the infusion with hydrochloric acid, the amount of reducing-sugar was found to be but 0.08 gram in 200 c. c. (1 small cupful) of the infusion, an amount entirely inconsequential when dealing with the quantities of urinary sugar ordinarily found in this research.

INFLUENCE OF MUSCULAR WORK UPON METABOLISM IN DIABETES.

As is well known, with normal individuals the slightest increase in muscular activity will result in an increase in both the excretion of carbon dioxide and in the intake of oxygen. Usually, with normal individuals, the increase in these gaseous products is essentially the same so that the relationship between the carbon dioxide and the oxygen, *i. e.,* the respiratory quotient, does not materially alter during muscular work. This has been shown in innumerable experiments made by Zuntz and his co-workers.

While our experiments were not primarily designed to study the question of the influence of muscular activity upon the respiratory quotient and on the character of the metabolism in diabetes, certain results were obtained which point towards rather interesting conclusions. With one of the subjects, Case C, an experiment was made with the respiration apparatus and immediately thereafter the subject entered the chair calorimeter for another experiment. It was noted that in one instance the respiratory quotients changed from 0.64, the average of a number of periods with the respiration apparatus, to 0.69, the average of three periods in the chair calorimeter. In the second instance, the average with the respiration apparatus was 0.71 and with the chair calorimeter 0.74. Both instances indicated, therefore, a slightly larger combustion of carbohydrate. In thus changing from the lying to the sitting position, greater muscular activity was introduced, and consequently the character of metabolism may have been affected. It is important, however, to note that small differences in the respiratory quotient may be accounted for by the differences between respiration of the lungs alone on the one hand, and that of the whole body, including the cutaneous respiration, on the other, for as Magnus-Levy has pointed out, the absence of the cutaneous respiration may lower the respiratory quotient from 0.01 to 0.015. This observation of Magnus-Levy, however, is made in large part upon theoretical grounds, and as yet has not been given complete proof.

In addition to the observation previously referred to, namely, the change from the respiration apparatus to the chair calorimeter, experiments were also made on two days in which the subject was asked, while still lying on the couch used with the respiration apparatus, to perform certain muscular movements in connection with his recumbent position. Both of these experiments showed a noticeable increase in the total metabolism as indicated by the carbon-dioxide excretion and the oxygen absorption, and there was also a slight increase in the respiratory quotient. In the first experiment he moved the arms frequently in handling a newspaper and also moved his legs frequently.

There was sufficient muscular activity to raise the pulse-rate from 52 to 58 per minute. In the second experiment, there was not only an increase in the total katabolism but also a marked increase in the respiration-rate. In this last experiment, instead of moving the arms about and handling a newspaper, he

was told to twitch the muscles continuously throughout the experiment, and this resulted in a marked increase in the metabolism. The pulse rose from 54 to 66. In neither case was the muscular exercise sufficient to affect the respiration-rate. The results of these two experiments on twitching the muscles and other muscular movements are given in table 189.

TABLE 189.—*Comparison of the gaseous exchange in rest and in work experiments with Case C. (Respiration apparatus.)*

Date.	Kind of experiment.	Number of periods.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.
1909.			*c. c.*	*c. c.*	
Oct. 30	Rest	3	160	228	0.70
	Work	2	178	253	.71
Oct. 31	Rest	4	161	232	.69
	Work	1	183	249	.73

From these observations it can be inferred that the muscular exercise was accompanied by the combustion of carbohydrate. There may be, therefore, three possible explanations:

First, there may be an increased ventilation of the lungs, causing an abnormal excretion of carbon dioxide, as was pointed out by Zuntz in connection with his respiration experiments, in which case the normal ventilation must be established before satisfactory results can be obtained; second, there may be a formation of acid in the body that expels the carbon dioxide, as pointed out by Mohr[1]; and, finally, there may be an actual combustion of carbohydrate.

Singularly enough, as measured by the carbon-dioxide excretion and oxygen consumption, the amount of work performed on both days during the working period was essentially the same. In the second experiment we have, however, a distinct increase in the respiratory quotient, which points strongly towards a consumption of carbohydrate during the period of work.

In these two experiments on the respiration apparatus, any increased ventilation of the lungs incidental to muscular work might cause a sweeping out of carbon dioxide from the system. The increased muscular activity resulting from the transition from the respiration apparatus to the chair calorimeter could not have produced such an effect, however, as the periods in the chair calorimeter were too long for the influence of any sweeping out of carbon dioxide to persist.

That the diabetic, even with his low storage of glycogen or carbohydrate, can actually supply this material for muscular work when occasion demands it has long been recognized. Nehring and Schmoll concluded that muscular activity in diabetics was also at the expense of glycogen from the fact that it was possible in many instances to reduce the sugar excretion by controlling the muscular activity.[2] This is also fully in accord with the experiments made by Mohr,[3] in

[1] Mohr, Zeitschr. f. Exp. Pathol. u. Therapie, 1907, **4**, p. 940.
[2] Nehring and Schmoll, Zeitschr. f. klin. Med., 1907, **31**, pp. 59–92.
[3] Mohr, *loc. cit.*, p. 939.

which he found with a diabetic dog that there was a noticeable increase in the respiratory quotient during walking, and therefore he concluded that diabetics can burn but little glycogen until there is the most urgent need for it. Under those conditions it can be oxidized, although very slowly. It is thus evident, even in some of the most severe cases of diabetes, that the capability for burning glycogen or carbohydrate is not entirely absent, and we may have here the condition indicated by von Noorden[1] when he said:

> One can not help thinking that, in man, even when death has resulted from coma, the diabetes has not always been quite "complete"—that is to say, the pathological processes which produce diabetes have not developed so far, and the factors which favor the storing up of glycogen have not been so completely removed, as is the case in a dog whose pancreas has been entirely ablated.

These observations do not agree with those reported by von Noorden[2] as having been made by Salomon in his laboratory. Salomon studied the respiratory exchange with two cases of severe diabetes, at rest, and after working or during work with an ergostat. While the working metabolism was some five or six times that of the resting metabolism, the respiratory quotient actually decreased in both instances, but the experiments are somewhat complicated in that they were not made in the morning without food but about 2 hours after a mid-day meal consisting of meat, vegetables, and 25 grams of butter and cheese.

Many practical difficulties are encountered in making experiments with muscular work in severe diabetes, as frequently the subjects are too weak to undergo work experiments, but it is obvious that physiology may learn much from such experiments, and we hope that further information on this line can be accumulated.

THE CALORIFIC EQUIVALENTS OF CARBON DIOXIDE AND OXYGEN.

The methods of indirect calorimetry have been developed for use with normal individuals so extensively that at present much of the information with regard to the energy transformations of resting man has been secured in this way. Until a sufficient number of experiments had been made, in which the three factors of metabolism were measured, we had no recourse but to compute the katabolism from the nitrogen excretion, the carbon-dioxide elimination, and the oxygen consumption, and then, from the well-known heat of combustion of protein, fat, and carbohydrates, to compute the energy in the katabolized materials, thus giving indirectly the heat-production. Recently, a large number of experiments on normal individuals have been reported by Benedict and Carpenter in which the calorific equivalents of carbon dioxide and oxygen, secured under different body-conditions, have been determined.

In diabetes, where the computation of the nature of the katabolized material is very much complicated by the abnormal cleavages of the materials of the

[1] v. Noorden, Metabolism and Practical Medicine, 3, p. 542, Chicago, 1907.
[2] v. Noorden, *loc cit.*, p. 584.

body, the indirect method of calorimetry has been used with but partial success. Since in the experiments here reported we have determined simultaneously the heat-elimination, the carbon dioxide, and the oxygen, it seemed desirable to find out if there were any definite relationships existing between these factors of metabolism. Since the katabolism was, in general, chiefly of fat, it is possible that at least the relationship between the carbon-dioxide and heat-eliminations may be relatively constant, and if so, a factor may be derived which may prove of value in interpreting the total energy transformations in many earlier experiments.

When starch is burned, for every gram of carbon dioxide produced, there are liberated 2.58 calories of heat, and for every gram of oxygen absorbed 3.55 calories of heat. In table 160, page 166, the calorific equivalents of both carbon dioxide and oxygen for a number of the principal food- and body-materials are given. It is seen that for fat the values are essentially the same for both carbon dioxide and oxygen, while with carbohydrate there is a much larger heat-production per gram of oxygen absorbed than per gram of carbon dioxide produced.

In experiments on man, by dividing the total heat-elimination by the number of grams of carbon dioxide, we obtained directly the calorific equivalent of carbon dioxide. A similar computation gives the value for the oxygen absorbed. The results for the experiments with diabetics have been computed, and an abstract given in table 190.

TABLE 190.—*Calorific equivalents of carbon dioxide and oxygen in experiments with diabetics in periods with and without food.*

[Average amounts.]

Subject.	Calorific equivalent of carbon dioxide.		Calorific equivalent of oxygen.	
	Without food.	With food.	Without food.	With food.
Severe diabetes.	*cals.*	*cals.*	*cals.*	*cals.*
Case A	3.41	3.42	3.36	3.43
B	3.25	....	3.40	....
C	3.46	3.37	3.37	3.26
E	3.47	3.32	3.47	3.19
F	3.44	3.27	3.50	3.31
G	3.03	3.47	3.06	3.66
H	2.97	....	3.13	....
I	3.24	....	3.31	....
J	3.09	....	3.17	....
Average of severe cases.	3.26	3.37	3.31	3.37
Light diabetes.				
Case K	3.59	....	3.77	....
L	3.26	....	3.44	....
M	3.42	....	3.59	....
Average of light cases.	3.42	....	3.60	....
Average of all cases	3.30	3.37	3.38	3.37

An inspection of the figures shows that in general the calorific equivalent of carbon dioxide is somewhat higher with the lighter cases of diabetes than with the severe cases, and the average of all cases is 3.30 calories without food, and in experiments with food, 3.37 calories. So far as diabetes is concerned, the calorific equivalent remains essentially the same whether food is taken or not. There is, however, a slight difference when the severe cases are compared and we find the calorific equivalent is somewhat lower with the severe cases without food than with food.

Considering the calorific equivalent of oxygen, the results are essentially the same as with carbon dioxide, namely, the highest calorific equivalent is found with the light cases. It seems to be immaterial whether food was taken or not with the severe cases so far as the calorific equivalent of oxygen is concerned, for it remained essentially the same in both cases.

It is also of interest to note that the number of calories accompanying the production of 1 gram of carbon dioxide is essentially the same as that accompanying the consumption of 1 gram of oxygen in diabetes, so that with accurate carbon-dioxide measurements, one can compute directly the heat-elimination by means of these factors. We can assume, then, that for every gram of carbon dioxide there will be produced without food 3.30 calories, and with food 3.37 calories.

These factors have a particular value inasmuch as a number of earlier writers on diabetes have given the total 24-hour amount of carbon-dioxide and have also attempted to compute indirectly the heat-production. We have computed here the heat-production given by these earlier investigators, using the value 3.37 as the calorific equivalent of carbon dioxide. The results are given in table 191, together with the amount computed either by the authors themselves or by others who have had occasion to use their values. In this table the figures for the earlier calculations of the experiments of Pettenkofer and Voit, Ebstein, Weintraud and Laves are taken directly from a table given by Magnus-Levy.

TABLE 191.—*Heat elimination of subjects in experiments made by earlier investigators on diabetes.*

Experimenter.	Body-weight.	Carbon dioxide eliminated per 24 hours.	Heat eliminated per 24 hours.			
			Calculated by earlier investigators.		Calculated by factor 3.37.	
			Total.	Per kilogram.	Total.	Per kilogram.
	kilos.	*grams.*	*cals.*	*cals.*	*cals.*	*cals.*
Pettenkofer and Voit	52.3	637	[1]1900	36.0	2147	41.1
Ebstein	61.2	688	2200	36.0	2318	37.9
Weintraud and Laves	64.0	719	[2]2400	37.0	2423	37.9
Dubois and Veeder	70.4	749	2453	34.3	2524	35.9

[1] Note by Magnus-Levy. *Loc. cit.*—Fritz Voit gives somewhat lower values. See Zeitschr. f. Biol., 39, 1892, p. 129.
[2] Note by Magnus-Levy. *Loc. cit.*—Estimated from the values for carbon dioxide eliminated which apparently are more reliable than the values for the oxygen consumed.

Magnus-Levy[1] has given the value of 3.31 calories per gram of carbon dioxide with normal individuals under conditions in which the respiratory quotient was 0.72. Since, with these diabetics, the average respiratory quotient was a little above this point, it is of interest to see how closely the value of 3.31 given by Magnus-Levy agrees with that actually found by experiments with the respiration calorimeter, *i. e.*, 3.37.

In a series of experiments reported by Johansson,[2] the carbon-dioxide excretion is given only for 1 hour's time. These values have been computed, using the calorific equivalent of carbon dioxide as 3.37, and the following values are found with the four subjects:

Subject E-k-n, with a body-weight of 61.8 kilograms, gave off 1545 calories in 24 hours, or 25 calories per kilogram in 24 hours; subject Str-ll, with a body-weight of 85 kilograms, gave off 1965 calories per 24 hours, or 23.1 calories per kilogram; Frau Sj-st, with a body-weight of 43.4 kilograms, gave off 1303 calories per 24 hours, or 30 calories per kilogram per 24 hours; Frau St-g, with a body-weight of 54.4 kilograms, gave off 1512 calories per 24 hours, or 27.8 calories.

From these results it is clear that the calorific requirement of Johansson's subjects was much less than those of the earlier investigators, a fact that is easily explained, since in Johansson's experiments the subjects were lying quietly with practically enforced muscular rest, while in the earlier investigations the subjects could move about in a large respiration chamber and the body-activity was unquestionably somewhat greater.

From the results of these experiments, therefore, it is obvious that in severe diabetes, where the tolerance for carbohydrate is very low and the respiratory quotient is not far from 0.70 to 0.72, the calorific equivalent of carbon dioxide, taken as 3.37, should give values for the total heat-production that are well within the limits of experimental error. The calorific equivalent of the oxygen in diabetes has not as great a value as that for carbon dioxide, for it is relatively seldom that the oxygen determination in diabetes can be made over a long period of time. The experiments made with the Zuntz-Geppert apparatus usually continue for but a few minutes, and it is only with the chamber method that we can secure a 24-hour oxygen consumption. In general, then, we may state that in cases of severe diabetes with respiratory quotients as low as 0.72, or diabetics with practically no carbohydrate tolerance, for every gram of carbon dioxide excreted there will be a liberation of 3.37 calories of heat.

[1] Magnus-Levy, Physiologie des Stoffwechsels, p. 245.
[2] Johansson, *loc. cit.*

GENERAL CONSIDERATIONS WITH REGARD TO THE INCREASED METABOLISM IN DIABETES.

Sufficient experimental evidence has accumulated to show that the metabolism in normal man is in general proportional to the body-weight; in other words, a large individual will give off a larger amount of heat than will a smaller individual. It is also well known that metabolism is affected by muscular activity, by the ingestion of food and by a rise in body-temperature, and in seeking an explanation for the increased metabolism noted in diabetics, it is important to consider all of these factors.

Psychical influences.—With the diabetic subjects who were unaccustomed to the laboratory and to the apparatus, a possible explanation of this increased metabolism may be that the novelty and the psychical influence played an important rôle. As a matter of fact, these subjects did not show any particular disquietude on going inside the chamber nor do any of our subjects, as a rule. One or two of the diabetics, as pointed out in the previous text, were extremely apprehensive and were distinctly nervous inside the chamber, but most of the subjects were very quiet and frequently went to sleep.

Muscular activity of diabetics as compared with that of normal individuals.—It may be contended that the increased metabolism noted with the diabetic subjects may be due to the fact that they were more restless and more muscularly active while inside the respiration apparatus. Furthermore, certain of the normal individuals were members of the laboratory force and had therefore become more or less "trained" subjects. It can be easily seen, however, that two of our diabetic subjects, Cases A and C, had a sufficient number of experiments made with them to become likewise "trained," but aside from this, it is a fact that the majority of the diabetics were extremely quiet inside the chamber, frequently falling asleep and having to be called, and at other times sitting quietly reading with minimum muscular exertion. They were very sick, and as a consequence were weak and disinclined to move around to any great extent. Furthermore, a careful comparison of the pneumograph curves made with these subjects and with the normal individuals shows that on the whole the diabetics were very much quieter than were the normal individuals.

While external muscular work may be eliminated in these comparisons, it is always possible that the pulse- and respiration- rates, which are the indices of the internal muscular work, may have been larger. A careful examination of all the records made in connection with these experiments shows that there was nothing abnormal whatever, even in the pulse-rate or respiration-rate of these individuals, save that Case I had an unusually high pulse-rate, and that Case A, during the experiments in the spring, had for him an abnormally high pulse-rate. Otherwise nothing abnormal was observed, and we have no reasons for believing that the pulse-rate as such, could influence in any way this increased metabolism. Unfortunately, blood-pressure observations were not made with

sufficient frequency to draw definite deductions. It is conceivable that while the pulse-rate did not change, the blood-pressure might have been higher, but we have no reason for believing this.

Body-temperature.—A careful examination of all the temperature records fails to show the influence of any possible slight temperature rise upon metabolism, although it is well known that the febrile temperature results in an increased metabolism. It is certain, therefore, that we can not explain the increased metabolism noted with diabetics on the ground of a febrile temperature.

Increase of protein katabolism in diabetes.—The possibility of the increase in gross metabolism in diabetics being due to an increased katabolism of protein with its specific dynamic action has been considered in detail in a preceding paragraph, where it was seen that although there is a slight increase in the total nitrogenous excretion of diabetics over the normal individuals, nevertheless the excess amount could not possibly account for more than 1 or 2 per cent of the total energy transformation; therefore, this possibility can be wholly excluded.

Food and drink.—No food was administered in the experiments which are compared to secure data regarding the fundamental metabolism of diabetics, and hence we have not the complicating factor of the influence of the ingestion of food upon metabolism to consider. The improbability that the small amounts of coffee infusion taken prior to the experiments influenced the metabolism in any way has already been pointed out.

Comparison of normal and diabetic individuals and the influence of differences in physical characteristics.—Apparently, therefore, there are no obvious external evidences of differences in the two classes of experiments to warrant an explanation of the increased metabolism on either the grounds of increased muscular activity, increased pulse- or respiration-rates, increased body-temperature, psychical disturbance, or an excessive protein katabolism. Food was not ingested in any case, and the possible influence of the previous ingestion of black coffee has been shown to be so slight as to be practicably negligible.

We have only to consider, then, the variations in the physical characteristics of the normal and diabetic individuals used in the comparisons. There are two methods by which these comparisons can be made. In the first place, one can select a diabetic with a given body-weight and height with whom the metabolism has been measured. We can then compare him with a normal individual of approximately the same body-weight and height, whose metabolism has also been measured, and note the differences in the metabolism. This method has been used by Magnus-Levy.[1]

Such a comparison involves two assumptions: First, that a normal individual can be found with the same body-weight and height as that of the diabetics; second, that the metabolism of the normal individual can be compared directly with that of the diabetic. With regard to the first of these assumptions, it is generally true that diabetics are more emaciated than normal individuals, and

[1] Magnus-Levy, Zeit. f. klin. Med., 56, 1905, p. 87.

that usually the body-weight is somewhat less than with normal individuals of the same height, and it is therefore difficult to select individuals with the same body-weight and height. Second, as a result of an examination of the results of the metabolism of normal individuals given in table 167, it is seen that there may be very noticeable differences in metabolism with normal individuals of approximately the same weight and height. This has been shown not only in the experiments made with the Zuntz-Geppert apparatus, but likewise in unpublished experiments of Benedict and Carpenter. If two individuals, such as subjects 9 and 10 in table 161, have the same body-weight and widely different metabolism, it is very important to know which of the two individuals is selected for comparison with diabetics, since with one individual a decreased metabolism may be shown, and with the other a highly increased metabolism. We believe that the normal metabolism of individuals has not been studied in a sufficient number of cases to permit of such a close comparison as this, namely, the study of the metabolism of diabetics as individuals and comparing them with normal individuals of the same weight and height. We further believe that the only logical method for comparison is to place diabetics in a large group and compare them with a group of normal individuals of approximately the same body-weight and height. This method has been followed in these experiments. This assumes that the values used as normal values are truly representative of an average group of individuals who may, with propriety, be compared to the group of diabetics studied.

As an index to the values found with the series of experiments designated as normal, we have compared these with results published by Benedict and Carpenter, and also with the results obtained with the Zuntz-Geppert apparatus. The results are given in table 192, in which it is seen that the average body-weight of all the subjects was not materially different in the three different sets of experiments. The average height was the same in both the published and unpublished material of Benedict and Carpenter. The carbon-dioxide excretion was essentially the same in all three cases, but the oxygen consumption is somewhat lower in the unpublished experiments of Benedict and Carpenter than in the other two instances. On the whole, the agreement of the results implies that the figures for the normal subjects here used are justified.

TABLE 192.—*Comparison of results of experiments with normal subjects at rest, in a reclining position.*

	Average body-weight.	Height.	Carbon dioxide elimination.	Oxygen consumption.
	kilos.	*cm.*	*c. c.*	*c. c.*
Benedict and Carpenter (unpublished experiments)	68.1	172	2.95	3.51
Benedict and Carpenter (published experiments)	66.6	172	3.01	3.75
Zuntz-Geppert apparatus	63.6	...	2.96	3.79

With normal individuals it has been found that, in general, the larger the body-weight the less the carbon-dioxide excretion and oxygen consumption per kilogram of body-weight. This is very well emphasized by table 161, copied from the published work of Zuntz and his co-workers given on page 168. The differences are especially noticeable when dealing with the higher and the lower weights, and have frequently been pointed out in the case of diabetics, a fat man usually showing a much lower metabolism per kilogram of body-weight than a thin man. While, theoretically, the metabolism on the basis of per kilogram of body-weight should be much the same with all individuals, it can be seen from the table just referred to that even with individuals of the same weight and height there may be marked differences. It is all the more important, therefore, when normal individuals are compared with diabetics, that there should be no discrepancy in the metabolism per kilogram of body-weight due to a difference in the average weight and height.

As a typical example, the results of experiments with diabetics in the chair calorimeter without food and with the normal individuals with whom they are compared have been computed. The average weight of all the diabetics was 59.9 kilograms, with an average height of 174 centimeters. The average weight of the normal individuals was higher (68.1 kilograms), while the height was 172 centimeters. Using this group as a whole, then, we have the tall diabetic with lighter weight compared with the shorter normal individual of somewhat heavier weight. According to the results reported by Benedict and Carpenter, the tall, lean individual has a tendency to a higher metabolism per kilogram of body-weight than the short, fat person. Under these conditions, therefore, we would expect to find a somewhat higher metabolism with the diabetics than with normal individuals. The normally occurring differences in metabolism between a group of individuals having the average weight of the diabetics here studied and normal individuals having the average weight of the normal individuals here studied may be found in a number of ways. If, instead of using the averages of a large group of individuals reported either by Zuntz, or by Benedict and Carpenter, we take a group of individuals varying from 64 to 72 kilograms in weight, and then another group varying from 56 to 64 kilograms in weight, we can obtain average values which will approximate those which would be obtained on normal individuals with the average body-weight of 60 kilograms and 68 kilograms. Calculations show that, in general, when groups are studied in this way the carbon-dioxide excretion is 3.16 c. c. per kilogram per minute with a body-weight of 60 kilograms, and 2.99 c. c. with a body-weight of 68 kilograms, and the oxygen consumption 3.96 c. c. at 60 kilograms, and 3.75 c. c. at 68 kilograms. Thus, there are differences indicating a slight increase in the metabolism per kilogram of body-weight with the lighter weight individuals. The differences are not, however, appreciable when compared with those found between the groups of diabetics and the normal individuals in table 179, page 193.

Still another possibility is to be considered if we are to concede what Magnus-Levy maintains, that the emaciation results in a disturbance of the relationship between the body-surface and the body-weight, so that these cases should be considered as having a body-weight and a metabolism equal to that in their original greatest weights in health. The arguments against this assumption of a relation between body-weight and body-surface have already been presented. If Magnus-Levy's assumption is correct, it is easily seen that the metabolism per square meter of body-surface should be the same with these diabetics irrespective of the body-weights, and as body-weight decreases the metabolism per kilogram should increase. On the other hand, with at least one of our cases, Case C, who was studied over a considerable period of time, there was a noticeable change in body-weight unaccompanied by a material alteration in the metabolism per kilogram of body-weight. An abstract of the results with this case is given in table 193.

TABLE 193.—*Metabolism per kilogram of body-weight in experiments without food with Case C.*

Date.	Body-weight.	Calorimeter experiments.			Respiration experiments.	
		Carbon dioxide per kilogram per minute.	Oxygen per kilogram per minute.	Heat eliminated per kilogram per hour.	Carbon dioxide per kilogram per minute.	Oxygen per kilogram per minute.
1909.	*kilos.*	*c. c.*	*c. c.*	*cals.*	*c. c.*	*c. c.*
Apr. 13	65.4	3.15	4.20	1.28	....	....
May 14	64.0	3.22	4.31	1.23	....	....
June 8	62.7	3.14	4.72	1.24	....	....
June 11	63.1	3.22	4.80	1.28	2.79	4.01
June 15	62.6	3.15	4.55	1.36	2.78	4.44
June 18	62.7	3.03	4.08	1.26	2.89	4.08
June 22	62.8	3.14	4.40	1.40	2.60	3.82
June 25	62.4	[1]2.95	[1]4.15	....	2.82	4.23
Aug. 24	60.0	....	....	....	2.78	3.93
Oct. 25	54.9	....	....	....	3.33	4.85
Oct. 26	54.9	3.24	4.54	1.26	3.04	4.28
Oct. 27	54.9	....	....	....	3.21	4.52
Oct. 28	54.9	....	....	....	2.92	4.44
Oct. 29	56.1	....	....	....	2.83	4.19
Oct. 30	56.1	....	....	....	2.85	4.06
Oct. 31	56.1	....	....	....	2.87	4.14

[1] Bed calorimeter.

On April 13, 1909, this subject had a body-weight of 65.4 kilograms, and the metabolism, as measured by the carbon-dioxide excretion, oxygen absorption, and heat-elimination, was not far from that of October 26 of the same year, when the body-weight was but 54.9 kilograms. There was a slight increase in the carbon-dioxide excretion, a noticeable increase in the oxygen consumption, and but a slight decrease in the heat-elimination. Unfortunately, but one calorimeter experiment was made with this subject in the fall. However, we have a series of respiration experiments made during the middle of June and a

long series in the latter part of October, so we have an excellent basis for comparison. It is seen from the results in the comparison of these experiments that there was essentially no difference in the metabolism of this subject during the two periods, although there had been a material change in weight, amounting to nearly 7 kilograms, or 10.7 per cent. Although there was this marked loss in body-weight, the metabolism per kilogram of body-weight was not altered, and apparently the heat-transforming power of the material was lost with it and not conserved by the body.

This experience is wholly in line with the observations first made by Zuntz and Lehmann, that with very long fasting experiments the metabolism per kilogram during complete rest without food was not materially altered. With the fasting experiments at Wesleyan University, while the total 24-hour transformation of matter gradually decreased during a 7-day fast, Zuntz has computed from the night period that there was no material decrease in the energy transformation while the subjects were at rest and asleep, thus showing that the two series of experiments fully substantiate each other. It is remarkable that with a loss of body-material such as is undergone through a long fast or through the ravages of diabetes, there should be a loss of the heat-producing power of the body, while on the other hand, as has been demonstrated on healthy men, there may be a very considerable storage, not only of fat but of nitrogenous material, without any increase in the oxidative powers of the body. Unfortunately, experimental evidence has not yet been sufficiently accumulated to show the difference in metabolism as measured on non-diabetic individuals of large body-weight who have subsequently lost flesh by reason of dietetic treatment or otherwise with a sufficient degree of accuracy to throw much light upon this point. Such experimental evidence is much to be desired and should be accumulated.

It seems proper, therefore, to contend as the result of the experiments with Case C that the loss of weight of diabetics is accompanied by a decrease in metabolism which is, relatively speaking, proportional to the body-weight so that the lower body-weight had a metabolism per kilogram of body-weight not much different from that of the higher weight. The highest weight during an experiment with this subject was 65.4 kilograms, and this was some 10 kilograms less than his greatest weight in health, but we have no evidence whatever as to the difference in metabolism between that of the best body-weight and that at 65.4 kilograms. It is more than probable that the kind of material lost when the body-weight fell from about 75 kilograms to 65.4 kilograms differed materially from that lost when the body-weight fell from 65.4 to 54.9 kilograms. In the first instance the material lost may not have been of active protoplasmic nature, and therefore vitally influencing metabolism, while in the second it evidently was of such a nature. Furthermore, with a loss of body-weight amounting to 20 kilograms on 75 kilograms, or about 27 per cent, one would expect, if there were to be a marked decrease in the surface, to find loose, flabby skin and other evidences of a former large body-area. As a matter of fact, nothing of this

kind could be noticed with this, or indeed, with any of the other subjects. While, as is well known, the relationship between the body-weight and the body-surface does vary materially between fat and thin people, nevertheless we have no reason for believing that with these diabetics there was a sufficient disturbance of the relationship to account for the marked differences in the metabolism noted with diabetics over normal individuals. It is obvious, therefore, that the experiments with Case C are to be taken as strong evidence against the theory that the increased metabolism noted in severe cases of diabetes is due to the fact that the body-surface is larger in proportion to the body-weight than with normal individuals.

Character of the metabolism during severe illness.—With Case A it was apparent that in the spring when he was most ill, the metabolism had a distinct tendency to be higher than at other periods of the year. The natural inference is, therefore, that the diminished vitality and general weakness resulted in a stimulation of the metabolism in an effort on the part of the body to make up for the lack of physical tonus. This was evident, not only from the increased pulse-rate, but likewise from a somewhat higher katabolism as a whole.

Of the other subjects we have but one, Case C, who was studied both during a period of grave illness and during periods when he was fairly comfortable. In the fall, about two months before his death, Case C was in a rather critical condition. At this time, contrary to the results with Case A, his metabolism was the same per kilogram of body-weight as it was in the spring when he was in fairly good condition. It is of unusual interest that although this patient's body-weight had fallen some 10 kilograms during the summer, nevertheless the katabolism per kilogram of body-weight remained essentially the same. It is to be noted, however, that the pulse-rate in the fasting experiment made in the fall was abnormally high (83), while 2 or 3 days later, during the oatmeal experiment, the pulse-rate decreased to 62, the former low level with this subject. With this abnormally high pulse-rate, one would have expected a somewhat higher metabolism than was actually measured with this subject. There is a possible explanation for this difference in metabolism in that with Case A the illness was due not so much to acidosis as to extreme weakness and debility. Under these conditions the stimulation of the heart was noticeable, the pulse-rate high, and the katabolism was also higher. On the other hand, with Case C, the illness was due chiefly to the severity of the acidosis, and possibly under these conditions the metabolism would take an entirely different course, but the acidosis with Case A was certainly not negligible.

The idea of an increased metabolism accompanying severe diabetes and extreme sickness is wholly at variance with the idea suggested by Naunyn, that there may be periods in the course of the disease during which time there is a very low metabolism. We see nothing here to justify the conclusion that these diabetics at any time showed an abnormally low metabolism, but on the contrary their demands were usually even individually higher than normal.

PRACTICAL CONSIDERATIONS.

It is important that diabetics should be given food containing a sufficient amount of energy, the idea that diabetics have a low energy requirement being obviously wrong. While with the ordinary normal individual it is possible to compute the food requirement with a reasonable degree of accuracy, with diabetics it is much more difficult, inasmuch as there is a considerable loss in the form of sugar in the urine; there is also the formation of unoxidized material, such as β-oxybutyric acid, in the urine, and it is necessary to take both of these factors into account. Practically every gram of sugar excreted in the urine results in a loss of 4.1 calories, and every gram of β-oxybutyric acid of 4.4 calories; consequently the diabetics who were excreting 100 grams of sugar per day and 20 grams of β-oxybutyric acid may have lost over 500 calories in this way. It is essential, of course, to make sure that the food ingested has an excess calorific content to make up for this deficiency.

It is also necessary to conserve the heat output of diabetics. They should not be exposed to undue cold or to severe wind, thus avoiding an increase of the excessive radiation of heat, and there should be the minimum amount of muscular work aside from a sufficient amount to maintain a generally good physical condition. In many cases one has literally to consider every individual calorie, as the reserve of body-material ordinarily used for excess demand has almost disappeared. Diabetics can not easily store fat or glycogen for an emergency, and therefore they should not be exposed to sudden or severe drafts upon body-material, as this has a tendency to deplete the storage, though, singularly enough, a fasting day has been demonstrated to be very beneficial in securing the removal of sugar and establishing a base line for the building up of a carbohydrate tolerance. The sudden appearance of coma after unusual exertion is, however, a well-known clinical fact.

In considering the energy output of diabetics, it is important, also, to note the energy required to warm urine. For example, if 3 liters of water are taken and excreted as urine in the course of the day, this water is warmed from an average of 10° C. to the temperature of the body, 37° C. In other words, each liter is warmed 27° C., and 3 liters thus warmed would result in the absorption of 81 calories. With a body-weight of but 42 kilograms, a weight not uncommon with many diabetics, this may be nearly 6 per cent of the total heat of a day, an amount that can not be neglected when practically every calorie must be taken into consideration in attempting to keep up the unequal fight of increased metabolism on the one hand and deficient utilization of carbohydrates on the other.

The possibility of the combustion of sugar formed from protein should be carefully noted. The non-nitrogenous portion of the protein molecule seems to be tolerated in many instances by diabetics better than preformed sugar. It is conceivable, for example, that it may be of distinct benefit to have larger amounts of protein ingested and thus have the carbohydrate moiety of the protein mole-

cule broken down, perhaps, in some different manner or different portion of the body than would be the case in the ordinary absorption of the carbohydrate from the intestine. Thus we deal here with two factors regarding the ingestion of meat. Without doubt, the ingestion of meat does stimulate the metabolism noticeably; this was observed even in the most severe cases of diabetes. That this stimulation of the metabolism is of actual benefit to the body is probable. If, in addition to the stimulated metabolism, we have the liberation of non-nitrogenous material in certain parts of the fluids of the body which may prove to be of special benefit, we have a double reason for the ingestion of large quantities of protein provided always that the patient can tolerate the protein and does not excrete the carbohydrate moiety of the molecule.

Even in severe cases of diabetes, the determination of the respiratory quotient may have great practical value in showing whether or not the subject is in a critical condition. If in experiments several hours after the last meal, the respiratory quotient is above 0.74, it is clear that there is a fairly liberal supply of glycogen or carbohydrate material stored in the body that is actually being burned. Each 0.01 point higher is, of course, more favorable. When practicable, therefore, the determination of the respiratory quotient without food may be of distinct value in rapidly diagnosing the severity of the case. It is furthermore possible that in many instances it is highly desirable to make a rapid diagnosis as the early treatment of a case may be of very great value. With the previously existing methods for determining the severity of the case, depending upon long-continued experiments with special diet, there may obviously be a period of time lost that is of vital importance to the patient in treatment.

The respiratory quotient may also be of very great value in determining the degree of tolerance of the individual for carbohydrate. It is impracticable in many instances to place patients upon an exact carbohydrate diet and be certain that the diet is followed. The tendency for many diabetics to unintentionally or intentionally deceive with regard to the amount of carbohydrates taken during a day is well known. If, however, a definite amount of carbohydrates be ingested and a definite increase in the respiratory quotient is found after a delay of 30 to 50 minutes, this may be taken as conclusive proof that there is an actual utilization of carbohydrate in the system. On the other hand, it has been frequently noted that there may be an ingestion of carbohydrate which under certain conditions does not appear in the urine and is still not actually burned, but which may be stored and subsequently excreted as sugar in the urine.

From the respiratory quotient, therefore, one should be able to form a tolerably clear idea of the situation. With a respiratory quotient of 0.70 or below, it is evident that the patient has practically no available carbohydrates, and if previously he has been living upon a moderately liberal diet, it is clear that the body has lost in a measure its power of storing any carbohydrate. We may naturally assume, therefore, that the patient may be in a serious condition. The replenishment or the building up of the storage of glycogen in the body may prove to be

a very important factor in the prognosis of diabetes and an indication of the advance in treatment.

Body-weight indications are very erroneous. On the basis of changes in body-weight, it requires some time to demonstrate the efficiency or the advantage of certain diets and certain methods of treatment, while by means of the respiratory quotient results can be obtained in a relatively short time. If carbohydrate is to be used in the body on being ingested, this can be shown by the respiratory quotient at once, while several days might elapse before positive proof could be obtained from the carbohydrate-balance as determined from the urine and the intake of food.

While the respiratory quotient, the dietetic treatment, the carbohydrate-balance, and the dextrose-nitrogen ratio would all point toward the presence in the body of the diabetic of a relatively small amount of glycogen, it is important for us to know, first, to what extent this glycogen storage exists, and second, to what extent it can be drawn upon or added to.

Many diabetics have a small storage of glycogen, and although not large, it is probably of vital importance. It is a serious question whether this storage should be materially depleted, and yet in an effort to secure sugar-free conditions in order to establish a basis for the development of a carbohydrate tolerance, it may frequently happen that this storage of glycogen is greatly depleted. In many instances, therefore, it is a question whether or not the attempt to make the patient sugar-free is wise. This point should be carefully watched and care taken not to draw too heavily upon the storage of glycogen. It is unquestionably true that some diabetic patients can never become permanently sugar-free, and, indeed, the attempt should never be made to bring them to this condition, since in the process of making the patient sugar-free, the storage of glycogen must be so seriously depleted that acidosis may quickly develop and the storage of glycogen can not be replenished. It becomes, therefore, a serious question as to whether it is not better in a large number of cases to have the patient with a low sugar-content in the urine and a fairly liberal supply of glycogen in the body rather than with no sugar in the urine and a very greatly depleted storage of glycogen.

INVESTIGATIONS NEEDED.

The topics for investigation here suggested represent only a few of the most pregnant which we hope soon to take up.

A series of 24-hour experiments is much needed in which the complete intake and output will be determined. Under these conditions it is possible to compute the kind of material katabolized and find to what extent the food ingested supplies the needs of the body. The storage of material and the retention of carbohydrate-material in the body can be definitely proved and a large number of questions which deal with the intermediary metabolism can probably be considerably illuminated by these experiments. A series of experiments, particu-

larly those including the ingestion of oatmeal, would be of unusual value, as any change apparent in the carbohydrate-balance would indicate a storage of large amounts of carbohydrate. If the carbohydrate was subsequently passed into the urine as sugar the balance will, as has been shown, tend to become minus again. On the other hand, if this material was stored during a portion of the day and subsequently oxidized, the respiratory quotient would be affected and it is possible that during the night, when the food ingested during the last meal of the day is drawn upon and the diabetic begins to feel the need of new material, the body might draw more heavily upon the storage of glycogen and thus affect the respiratory quotient.

By experiments of this kind we could demonstrate quite thoroughly the value of the various kinds of carbohydrate and protein food, as it is conceivable that with certain subjects the non-nitrogenous portion of the protein molecule may be really of considerable benefit in supplying energy in an otherwise scanty and rather monotonous diet.

Of considerable importance from the standpoint of physiology is the influence of the abnormal metabolism upon the specific dynamic action of the protein. It is conceivable, for example, that when the storage of glycogen is low and meat is given, the non-nitrogenous portion of the protein molecule may be converted to glycogen and not burned but stored, and consequently the so-called specific dynamic action might fail to appear. Thus we might have here a possible explanation of the specific dynamic action of protein in that the non-nitrogenous material of the protein is burned under conditions that give rise to special heat-production.

In studying the influence of the ingestion of protein and comparing the influence of the different kinds of protein, it may be advisable to note the value of ingesting the daily quota of this nutrient not in one but in several meals, so as to get the value of the stimulated metabolism throughout the whole day. On the other hand, it may be found of advantage to give the total protein quota in one meal and thus obtain an unusually large stimulation. Furthermore, whether this stimulation should be given at night or in the morning may be of significance. While large amounts of gelatine are not easily consumed as a rule, it is not entirely impossible that the use of gelatine in diabetes may be of value, and that the non-nitrogenous portion is converted to sugar which can be more easily burned or stored than the sugar formed from the ordinary protein, and although the nitrogen-sparing power of gelatine is lower than that of ordinary protein, it is not entirely absent. The important factor here is to secure a supply of energy which may be utilized by the body and also to secure a stimulating effect as a result of the specific dynamic action. Consequently, the lower protein-sparing power of gelatine is without special significance in this case.

If diabetics can be given a creatine-free diet or a meat-free diet it may be of value to study the simultaneous output of nitrogen, dextrose, and creatine, particularly on green days and on true fasting days. As the creatine in all probabil-

ity is derived from the breaking down of muscular tissue, some idea of the dextrose-nitrogen ratio and muscular tissue disintegration may possibly be obtained by this means. Unfortunately, the Folin method for determining creatine has not yet been proved to be accurate in the presence of many of the partially oxidized compounds existing in the urine.[1] If it could be experimentally demonstrated that known quantities of pure creatine added to diabetic urine could be recovered and found by the Folin method, this would make possible an interesting study upon the excretion of creatine in diabetes during a period of time when possibly no meat or creatine-producing material is eaten. Even in a 24-hour fast the creatine excretion might prove of very great interest.

The utilization of alcohol in a diet is also important, for if there is a disease in which the use of alcohol as a food is justified, that disease is diabetes. Energy studies should be made in which carbohydrates, fat, or protein should be replaced by alcohol to see to what extent the latter is oxidized, how rapidly it can be burned, if the respiratory quotient is immediately affected by its use, and if it in any way increases the metabolism as a whole. The influence of the ingestion of alcohol in varying amounts and in varying combinations with other nutrients may also be studied with both the large and the small respiration apparatus, and if subjects are used with diabetes of differing degrees of severity, results of great theoretical and practical value should be obtained.

[1] During a recent visit of one of us to the laboratories of Scotland, it was observed that considerable unpublished research of great interest in this connection was being conducted independently by Cathcart of Glasgow and Cramer of Edinburgh.